THE UNIVERSITY *of* EDINBURGH

Controlling endemic disease in cattle populations: current challenges and future opportunities

Maureen Carolyn Gates

Thesis submitted for the degree of Doctor of Philosophy
University of Edinburgh
2013

Declaration

I declare that the research within this thesis is my own work and any assistance received has been duly acknowledged. The work described has not been submitted for any other degree or professional qualification.

Maureen Carolyn Gates
Edinburgh, October 2013

Lay summary

Cattle are infected by a wide range of endemic diseases that undermine production and have detrimental effects on human, animal, and environmental health. Controlling these diseases is important, but challenging, due to the large number of potentially infectious contacts between cattle herds, the lack of affordable and accurate diagnostic tests to identify infected cattle, and the difficulty in motivating farmers with diverse priorities to take collective action against the spread of disease. With the increasing availability of high-resolution demographic data and high-performance computing, researchers have an unprecedented opportunity to study how these diseases interact with modern production systems and to develop more cost-effective strategies for controlling disease at the industry level. In particular, this thesis has shown that modifying individual farm management practices to reduce the number of cattle movements (a 'bottom up' approach) and introducing trade restrictions to alter key epidemiological features of the industry contact structure (a 'top down' approach) have significant potential to control multiple endemic diseases simultaneously as well as to improve farm profitability. However, there are still significant gaps in our knowledge of these complex systems. Any intervention that imposes financial or logistical constraints on cattle production has the potential to reshape industry contact patterns in unexpected ways as famers try to minimize the impact of regulatory changes on their business. Furthermore, the epidemiological landscape in which these diseases persist is expected to change through the widespread effects of environmental change, agricultural subsidization reform, and public opinion on modern production practices. There is a strong need both for further research into the socioeconomic factors driving farmer behaviour to better inform traditional epidemiological models and for close collaboration with industry stakeholders to ensure the research outputs are delivered in an accessible and user-friendly fashion.

Abstract

The British cattle population hosts a diverse community of endemic pathogens that impact the sustainability of beef and dairy production. As such, there has been a tremendous amount of ongoing research to develop more cost-effective strategies for controlling disease at the industry level. Cattle movements have come under particular scrutiny over the past decade both because of their role in spreading many economically important diseases and because the movements of individual cattle in Great Britain have been explicitly recorded in a centralized electronic database since 1998. Numerous studies have shown that these cattle movements organize into complex networks with key structural and temporal features that influence transmission dynamics. Building on previous work, this thesis used a variety of epidemiological and statistical models to highlight limitations in the current approaches to controlling disease as well as opportunities for reducing endemic disease prevalence through targeted interventions. Empirical disease data from the national bovine tuberculosis (bTB) control programme and from two seroprevalence studies of bovine viral diarrhoea virus (BVDV) in Scottish cattle herds were used in conjunction with movement data from the Cattle Tracing System (CTS) database.

Endemic diseases are often challenging to control due to lack of affordable and accurate diagnostic tests as well as the presence of subclinically infected carriers that can easily escape detection. There was evidence that combined issues with the sensitivity and specificity of routine surveillance methods for bTB were contributing to a low level of disease transmission within and between Scottish cattle herds from 2002 to 2009. For BVDV, herds that purchased pregnant beef dams, beef dams with a calf at foot, and open dairy heifers were significantly more likely to be seropositive even though these movements were responsible for only a small number of network contacts. In both cases, targeting the subset of high risk movements with disease specific biosecurity measures may be a more cost-effective use of limited national disease control resources.

Other researchers have suggested that control strategies should target multiple diseases simultaneously to reduce trade-offs in resource allocation. Using

key indicators of herd reproductive performance derived from the CTS database, it was shown that improving the reproductive management of herds operating below industry standards could reduce endemic disease prevalence by reducing the movements of replacement breeding cattle. A series of network generation algorithms were also developed to study the effects of restricting contact formation based on key demographic and network characteristics of actively trading cattle farms. Strategies that increased network fragmentation either by forcing highly connected farms to form contacts with other highly connected farms or preventing the formation of movements with a high predicted betweenness centrality were found to be particularly effective in limiting disease transmission.

For these models to be useful in guiding future policy decisions, it is important to incorporate financial and behavioural drivers of dynamic network change. Following the introduction of pre- and post-movement testing requirements for cattle imported into Scotland from endemic bTB regions, there was a significant decline in cross-border movements, which has likely contributed to the decreasing risk of bTB outbreaks as much as testing itself. Many endemic cattle diseases such as BVDV also spread through local transmission mechanisms, which may undermine the success of disease control programmes that exclusively target cattle movements. There was also evidence that in the absence of national animal legislation, few farmers were likely to adopt biosecurity measures against BVDV. This may be related to the perceived inefficacy of recommendations as well as general unawareness of farm disease status due to the non-specific clinical signs of BVDV outbreaks.

Although the CTS database was originally intended for use in slaughter traceback investigations, results from this thesis show how the basic records of births, deaths, and movements can be used to generate valuable insights into the epidemiology of endemic cattle diseases. The findings also emphasize that the management decisions of individual herds can have a substantial impact on industry level transmission dynamics, which offers unique opportunities to develop novel and more cost-effective disease control programmes.

Acknowledgements

It seems somehow wrong to declare that this thesis is my work alone when so many people have provided me with invaluable support and guidance over the past three years. I first owe a tremendous amount of gratitude to my primary supervisor, Mark Woolhouse, for constantly challenging me to step outside my comfort zone and never letting me settle for good enough when I had the potential to do so much better. Without his continued patience and constructive feedback, it would not have been possible to complete this thesis nor would I have gained so much valuable research experience. Mariano Ciccolini had the misfortune of being a post-doc here when I was first learning how to program and I am eternally grateful for his help in debugging obscure coding errors. I also wish to thank Victoriya Volkova for her hard work in liaising with the government agencies to obtain the cattle movement data and bovine tuberculosis surveillance data that formed the bulk of my thesis. Her help in interpreting the study findings was also invaluable. I was privileged to work with Roger Humphry on the bovine viral diarrhoea virus data and appreciate all his helpful feedback on the analyses and manuscript drafts. George Gunn was instrumental in arranging access to these data. I am also grateful to several anonymous reviewers for providing thoughtful remarks on the analyses that were submitted for publication. This thesis made significant use of the resources provided by the Edinburgh Data and Compute Facilities (ECDF) and I owe Sujai Kumar a huge thanks for walking me through how to use the computing cluster. My thesis was funded through the Principal's Career Development scholarship and the Scottish Overseas Research Student Award Scheme (SORSAS). I also wish to acknowledge EPIC for providing additional financial support for my research endeavours. Finally, I thank everyone in Epigroup and Ashworth for creating such a supportive environment to deal with the many challenges of being a PhD student.

Table of contents

List of abbreviations

AHVLA	Animal Health and Veterinary Laboratory Agency
BCMS	British Cattle Movement Service
BHV	Bovine Herpesvirus
BSE	Bovine Spongiform Encephalopathy
bTB	Bovine Tuberculosis
BHV	Bovine Herpesvirus
BVDV	Bovine Viral Diarrhoea Virus
CAP	Common Agricultural Policy
CI	Confidence Interval
CPH	County Parish Holding number
CTS	Cattle Tracing System
DEFRA	Department of Environment, Food, and Rural Affairs
EEC	European Economic Council
EU	European Union
FMD	Foot and Mouth Disease
GB	Great Britain
GLM	Generalized Linear Model
GSCC	Giant Strongly Connected Component
OR	Odds Ratio
OTF	Officially Tuberculosis Free
PAF	Postal Address File
PI	Persistently Infected
PTI	Parish Testing Interval
RADAR	Rapid Analysis and Detection of Animal-related Risks project
RHT	Routine Herd Test
R_e	Effective reproduction number
R_0	Basic reproduction number
SD	Standard Deviation
SICCT	Single Intradermal Comparative Cervical Tuberculin Test
SOA	Sole Occupancy Authority
UK	United Kingdom
VLA	Veterinary Laboratory Agency
ZINB	Zero-inflated Negative Binomial Regression Model

Chapter 1

General introduction

Background

With the human population projected to reach 9 billion by the year 2050, there is tremendous pressure on livestock production systems worldwide to find more sustainable and economical means of increasing production capacity (Thornton, 2010). Infectious disease management will play a crucial role in these efforts because of the well-established effects of livestock pathogens on human, animal, and environmental health. As well as causing direct production losses for the livestock industry through reduced animal performance, poor fertility, and higher culling rates, many infectious livestock diseases are also directly transmissible to humans, which carries important public health implications (Slingenbergh et al., 2004). At the same time, factors such as environmental change (Jones et al., 2013), agricultural subsidization reform (Dunne et al., 2001), public opinion (White and Whiting, 2000), antimicrobial resistance (Oliver et al., 2011), and animal welfare concerns (Webster, 2001) are changing the socioeconomic and epidemiological landscape in which these diseases persist.

There is a strong need for formal quantitative approaches to understand the complex interaction between pathogens and the livestock production environment (Woolhouse, 2011). Recent literature on infectious disease dynamics in livestock production systems has been heavily biased towards exotic and emerging pathogens. This is primarily because these can spread rapidly through naïve populations and cause significant financial losses through the resulting trade restrictions and eradication efforts. A classic example is the 2001 foot-and-mouth disease (FMD) outbreak in the United Kingdom, which resulted in the slaughter of over 7 million animals and cost the agricultural industry more than £8 billion in direct control expenditures, compensation for slaughtered animals, and lost marketing opportunities (Thompson et al, 2002). Consequently, there have been considerable

efforts to review the epidemiological models underpinning previous control decisions (Green and Medley, 2002; Savill et al., 2007; Tildesley et al., 2008), to assess the risk of future disease outbreaks (Robinson et al., 2007; Tildesley et al., 2011), and to develop alternate control strategies for reducing their financial impact (Tildesley et al., 2006; Schley et al., 2009).

Endemic diseases have historically received much less attention both because the effects of disease outbreaks are not as readily apparent (Carslake et al., 2011) and because many people also believe that endemic diseases are only a concern for farms that manage their livestock badly (Heffernan et al., 2008). However, as work by Bennett and colleagues (1999a) shows, the costs of preventing and controlling endemic disease in the British cattle industry alone can range from £275 million to £700 million per annum depending on the estimates used for disease prevalence. Furthermore, as an increasing number of countries achieve disease-free status through national eradication programmes, there are likely to be more restrictions on international livestock trade with the potential to limit future market opportunities (Leslie and Upton, 1999). Developing cost-effective strategies to control endemic diseases in cattle populations is therefore just as important, but comes with its own unique set of challenges.

The main objectives of this review were (1) to highlight key features of endemic diseases and modern production systems that act as barriers to disease control, (2) to provide an overview of current strategies for controlling endemic disease at the industry level, and (3) to describe how insights gained from empirical and theoretical studies can be used to develop more sophisticated approaches to endemic disease modelling and control.

Endemic cattle diseases

Cattle are infected by a diverse community of endemic diseases that spread between herds through the movements of infectious animals, personnel, equipment, and wildlife (Mee et al., 2012). A list of the major endemic cattle diseases along

with their causative agents and primary impact on production is presented in Table 1.1. Although each of these diseases has a unique epidemiology, they share many broader characteristics that impede diagnosis, treatment, and control.

Table 1.1: Summary of economically important endemic cattle diseases and their primary impact on production.

Common name	Pathogen(s)	Duration	Zoonotic risk	Primary impact
Bovine tuberculosis	*Mycobacterium bovis*	Chronic	Yes	Involuntary culling
Johne's disease (paratuberculosis)	*Mycobacterium avium* spp. *paratuberculosis*	Chronic	No†	Involuntary culling
Bovine viral diarrhoea virus	*Bovine viral diarrhoea virus*	Acute	No	Abortion
Contagious mastitis	*Staphylococcus aureus* *Streptococcus agalactiae* *Mycoplasma* spp.	Chronic		Reduced milk yield
Bovine respiratory disease complex	*Bovine parainfluenza 3* *Bovine respiratory syncytial virus* *Bovine herpesvirus1* *Mannheimia haemolytica* *Pastuerella multocida* *Mycoplasma* spp.	Acute	No	Treatment costs
Calf enteritis (scours)	*Bovine coronavirus* *Bovine rotavirus* *Cryptosporidium parvum* *Salmonella* spp. *Escherichia coli*	Acute	Yes/No‡	Treatment costs
Leptospirosis	*Leptospira hardjo*	Acute	Yes	Abortion
Neosporosis	*Neospora caninum*	Acute	No	Abortion
Enzootic bovine leukosis	*Bovine leukaemia virus*	Chronic	No	Involuntary culling
Digital dermatitis	*Treponeme* spp.	Acute	No	Treatment costs

† There is inconclusive evidence linking Johne's disease to Crohn's disease in humans (Grant, 2005).
‡ Bovine coronavirus and bovine rotavirus have no known zoonotic potential.

Clinical effects

Endemic cattle diseases present with a wide range of clinical manifestations varying from mild asymptomatic infections to severe life-threatening clinical episodes. In many cases, the only indication that disease is present in a herd is a general reduction in growth rates, milk yields, or animal fertility. These signs are non-specific and can all be influenced by other non-infectious causes of poor performance such as heat stress (West, 2003), dietary change (Owens et al., 1995), facility design (Caraviello et al., 2006), reproductive management (Grohn and Rajala-Schultz, 2000), and calf husbandry (Uetake, 2013). Consequently, farmers may not be aware of their herd's disease status unless routine diagnostic testing is performed. Furthermore, if the clinical effects on performance are mild, farmers may not perceive any benefit to eradicating disease from their herds. In both scenarios, these herds represent potential reservoirs of disease for other susceptible herds in the industry.

Diagnostic testing

The accurate diagnosis of infected animals and herds is a prerequisite for controlling infectious disease in cattle populations. Since endemic diseases can rarely be diagnosed through clinical signs alone, this most often requires some form of laboratory testing. For bovine tuberculosis (de la Rua-Domenech et al., 2006; Schiller et al., 2011), bovine paratuberculosis (Nielsen and Toft, 2008; Bastida and Juste, 2011), and contagious mastitis (Yancey Jr, 1999; Fox et al., 2005) in particular, the lack of sensitive and specific diagnostic tests has been highlighted as one of the major barriers to disease eradication. For endemic diseases in general, the presence of maternal antibodies, the use of non-marker vaccines, and co-infections with other pathogens can also interfere with the interpretation of antibody-based diagnostic tests (Brinkhof et al., 1996; Aranez et al., 2006; Houe et al., 2006; de Faria Naves et al., 2012). This inherently reduces the efficacy of disease control strategies based on testing purchased cattle to remove subclinically infected carriers

or sourcing purchased cattle from reportedly disease-free herds (Van Winden and Pfeiffer, 2008; Van Winden et al., 2011).

Treatment options

Another complicating factor in endemic disease control is the lack of effective treatments options for test-positive cattle. Currently, the only means of eliminating carriers for bovine herpesvirus, bovine tuberculosis, bovine paratuberculosis, bovine leukosis, and bovine viral diarrhoea virus is through slaughter. Compensating farmers for animals slaughtered for disease control purposes was one of the major expenses in the Swiss bovine herpesvirus eradication programme (Ackermann et al., 1990) and accounted for approximately one third of the total bovine tuberculosis control costs in the United Kingdom from 2009 to 2010 (DEFRA, 2012). The lack of indemnity payments for other endemic cattle diseases may discourage farmers eradicating disease in their herds (Gramig et al., 2009).

Cattle production systems

Historically, there has been a strong tendency to treat endemic diseases as a herd-level problem. However, as recent epidemics have made abundantly clear, cattle herds do not exist in isolation and there are many opportunities for disease to spread from infected herds through the direct movements of animals, personnel, and equipment as well as through other indirect local transmission mechanisms. Such contact has become virtually unavoidable in modern production systems as herds have become increasingly specialized to capture economies of scale and increasingly reliant on professional support services to handle the accompanying management challenges. In some cases, the risk of disease transmission can be mitigated through biosecurity measures, but there is often little quantitative evidence to prove their efficacy.

Cattle movements

Farmers routinely buy and sell cattle to maximize the returns on their available farm resources. These decisions are often motivated by complex factors such as the farm management and grazing capacity (Magne et al., 2011), current or projected market prices for cattle (Aadland, 2004), agricultural subsidy schemes (Veysset et al., 2005), and animal health regulations (Velthuis and Mourits, 2007). Poor herd management can also have a strong influence on the need to purchase cattle as well as the total number of cattle purchased. For example, breeding herds with low fertility or high heifer culling rates may not be able to maintain herd size through internal replacement alone (Tozer and Heinrichs, 2001; Caldow et al., 2005). Auction markets have a key role in facilitating livestock trade, but are also responsible for amplifying the risk of disease spreading through the cattle industry. Movements through auction markets occur over much greater distances than direct farm-to-farm movements and cattle sent to market from a single holding are often dispersed to multiple premises (Robinson and Christley, 2007). There is also the potential for disease to spread directly between cattle that are temporarily located at markets, showgrounds, and common grazing pastures.

Farm visitors

The intensification of cattle production systems has been accompanied by new management challenges that require technical expertise and equipment beyond what most individual farmers can reasonably provide. Consequently, there has been tremendous growth in livestock support services with many farmers routinely contracting veterinarians, artificial insemination technicians, nutritionists, hoof trimmers, equipment managers, commodity companies, and dead stock collectors to manage specialized aspects of animal care (Sanson et al., 1993; Nielen et al., 1996; Brennan et al., 2008). These individuals or companies often visit multiple animal holdings in a single day, which carries the risk of spreading disease if appropriate biosecurity measures are not taken to ensure that clothing, vehicles, and equipment

are properly decontaminated between farm visits (Bates et al., 2001; van Schaik et al., 2002; Ellis-Iversen et al., 2011).

Local transmission

Proximity to infected herds is an important risk factor for many endemic diseases (Perez et al., 2002; Ersbøll et al., 2010; Ohlson et al., 2010); however, the precise mechanisms of disease transmission are often poorly understood and multifactorial. Contact between neighbouring herds can occur through a variety of mechanisms including shared equipment or facilities (Brennan and Christley, 2012), the use of common grazing pastures (Rossmanith et al., 2005), airborne transmission (Mars et al., 1999), contaminated water sources (Halliday et al., 2006), wildlife reservoirs (Griffin et al., 2005), land application of manure (Ramírez-Villaescusa et al., 2010), and shared farm boundaries that permit direct nose-to-nose contact (Abernethy et al., 2011). These contact routes are the most challenging to regulate from a disease control perspective due the real or perceived costs, inefficacy, and impracticality of the recommended biosecurity measures (Bennett and Cooke, 2005).

Current control approaches

The collective impact of modern farming practices on the persistence of endemic diseases is often described using the effective reproduction number (R_e). This quantity measures the average number of secondary cases arising from a single infected individual interacting with a partially immune population over the course of its infectious period (Anderson and May, 1991). For veterinary epidemiologists, the particular goal and challenge lies in finding interventions that can be applied cost-effectively across the large population of cattle farms to reduce R_e sufficiently below one. This can rarely, if ever, be achieved through voluntary farmer compliance alone. Current approaches to controlling disease at the industry level usually involve a combination of (1) reducing the number of potentially infectious contacts

through targeted movement restrictions, (2) reducing the probability of disease transmission occurring through contacts by improving biosecurity, (3) reducing the duration of the average farm infectious period through herd-level eradication measures, and (4) reducing the proportion of susceptible farms through herd vaccination. Data collected from national livestock traceability systems in the European Union have provided researchers with a valuable framework for evaluating the relative costs and benefits of these available disease control alternatives.

Voluntary disease control

In most countries, farmers have the discretion to choose how endemic diseases are prevented and controlled on their farms. One of the most widely recommended biosecurity measures is to maintain a closed herd and, in situations where that is unfeasible, best practice guidelines dictate that all purchased cattle should either be sourced from disease-free herds or quarantined and tested after purchase (Moore et al., 2008; Mee et al., 2012). Although these measures are highly effective in preventing between-herd transmission (Chi et al., 2002), relatively few farmers adopt them in practice. In a survey of Wisconsin dairy farmers, almost half of the respondents purchased cattle, but only 49% routinely performed diagnostic tests before introducing them to the herd (Hoe and Ruegg, 2006). Similar findings have been reported in other survey studies (Faust et al., 2001; Wells, 2001; Brennan and Christley, 2012) with the proposed explanations being the lack of appropriate facilities to isolate cattle, the low perceived risk of disease introductions, the belief that testing and quarantine is ineffective, and the costs associated with testing, especially when large numbers of animals are purchased from multiple sources (Meuwissen et al., 2001; Flaten et al., 2005; Bennett, 2009; Ellis-Iversen et al., 2010).

There are also significant issues with compliance even when farmers adopt biosecurity measures or enrol in voluntary herd health schemes. For example, it

would be logical to assume that infected animals would be immediately culled to prevent disease transmission. However, a small pilot study from California found that most dairy producers actually kept cattle that tested positive for bovine leukaemia virus after purchase despite being aware of the risks to their herd (Moore et al., 2009). The most likely explanation is that farmers receive no indemnity for slaughtering infected cattle to control disease (Gramig et al., 2009) and there is currently no legal recourse against farms that sell infected cattle. The same farmers also reported that they would not have purchased the animals had they known the disease status in advance. As another example, Ridge and colleagues (2005) audited 54 Australian dairy herds participating in a Johne's disease control program and found that only 10 herds complied with all three recommended calf management practices. Similarly low compliance rates were reported in a voluntary survey of 534 from the same region of Australia, although it is worth noting that farms with a history of Johne's disease were significantly more likely to adopt recommendations than disease free farms (Wraight et al., 2000).

National control programmes

There is a strong need for collective action amongst farmers to control the many endemic diseases affecting the cattle industry (Bicknell et al., 1999), yet such efforts are still relatively rare. Carslake and colleagues (2011) attributed this to the fact that most endemic diseases have a low political profile. With a limited budget available for animal disease control, governments tend to prioritize resource allocation to diseases with immediate threats to public health or international trade. Bovine tuberculosis has received particular attention in the European Union (Gordejo and Verneersch, 2006) because of its direct zoonotic potential and ability to establish endemicity in wildlife populations. Several countries have also implemented eradication programmes against bovine viral diarrhoea virus (Greiser-Wilke et al., 2003) and bovine herpesvirus 1(Ackermann and Engels, 2006) due to

the significant effects of these diseases on animal production as well as the availability of effective control interventions.

In general, most eradication programmes are based on identifying infected herds through routine surveillance and then implementing measures to prevent further disease spread such as slaughtering infected cattle or issuing movement restrictions. These control measures are usually disease specific and applied uniformly across the population of cattle herds despite tremendous variation in the individual herd-level risk of acquiring and spreading disease. There is a potential for significant cost savings by developing strategies that are effective against multiple pathogens simultaneously and by tailoring the disease interventions to the unique epidemiological situation of each farm (Carslake et al., 2011). In particular, there has been growing interest in using risk-based surveillance to allocate disease control resources more cost-effectively at the industry level (Stark et al., 2006; Nöremark et al., 2011; Bessell et al., 2013). Answering these kinds of epidemiological questions requires detailed information on the demographic characteristics of individual herds, risk-factor models that can be scaled to the industry level, and a framework for simulating disease control scenarios.

Livestock traceability systems

Animal identification and traceability systems are an important part of national disease control programmes because they provide authorities with a rapid means of tracing the movement history of animals that were infected or exposed during a disease outbreak (Caporale et al., 2001). The European Union has been a forerunner in establishing global standards for livestock traceability systems. These efforts were primarily motivated by the need to restore consumer confidence in the safety of livestock products following the bovine spongiform encephalopathy (BSE) crisis in the United Kingdom during 1996. In the landmark Council Regulation (EC) No 820/97 introduced in April 1997, all member states were required to maintain a system that used ear tags to individually identify animals, computerized

databases to record demographic and movement for individual cattle, animal passports to remain with the animal from birth to death as a permanent record of movement history, and individual registers kept on each holding as a permanent record of potentially infectious contacts. This was replaced by Council Regulation (EC) No 1760/2000 in July 2000, which included more detailed regulations on compulsory beef labelling systems.

Although these databases were originally intended for use in contact tracing, they have also provided researchers with the unprecedented opportunity to study the spread of infectious disease at the industry level. For example, movement records from the United Kingdom have been used to explain epidemiological patterns observed in the 2001 foot-and-mouth disease outbreak (Green et al., 2006; Ortiz-Pelaez et al., 2006), to characterize the relative importance of local and long distance spread in the epidemiology of bovine tuberculosis (Gilbert et al., 2005; Green et al., 2008), to describe the metapopulation dynamics of *E. coli* O157 infections in cattle herds (Liu et al., 2007), to develop models of bovine viral diarrhoea virus control (Tinsley et al., 2012), and to conduct risk-factor analyses for a wide range of endemic diseases (Green and Cornell, 2005; Ortiz-Pelaez and Pfeiffer, 2008; Garcia Alvarez et al., 2011). Additionally, these databases provide valuable time series data on the demographic structure of the cattle industry that can be used to explore trends in cattle numbers, herd numbers, and marketing practices (Robinson and Christley, 2006; Robinson and Christley, 2007; Vernon, 2011) .

Insights from network theory

Until recently, ‘compartmental’ or ‘mass-action mixing’ models were widely used to study the spread of infectious disease through cattle populations and to evaluate the benefits of different disease control strategies. However, although these models are computationally attractive, the assumption that the population of farms is homogenously mixed and that every farm has an equal chance of spreading disease to every other inherently limits their epidemiological value. As analyses of national

cattle movement databases have shown, the probability that animals from any two farms will come in contacts depends on complex factors such as herd production type, geographic distance, and available marketing channels (Ezanno et al., 2006; Lindström et al., 2009; Nöremark et al., 2009; Aznar et al., 2011; Rautureau et al., 2010). Furthermore, a small number of farms with a disproportionately large number of contacts are often responsible for driving transmission dynamics at the population level (Woolhouse et al., 2005; Volkova et al., 2010). Consequently, social network analysis has emerged as a popular framework for studying the relationships between individual farms in a population and their implications for infectious disease control (Martínez-López et al, 2009b). This approach has provided many valuable insights that can be used to develop more cost-effective strategies for controlling disease in the future.

Network terminology

Reflecting its origins in mathematical graph theory, the elements of a network are referred to as *nodes* or *vertices*, while the relationships between them are referred to as *edges* or *contacts*. When the relationships are unidirectional, such as the movements of cattle from a source herd to a destination herd, the network is said to be *directed*. When the relationships are bidirectional, such as the nose-to-nose contact of cattle through fencelines, the network is said to be *undirected*. Node *degree* measures how many direct contacts a farm has with others in the network. In directed networks, degree can be further partitioned into *in-degree* and *out-degree* representing the number of potential sources and sinks for disease transmission, respectively. The degree of separation between any given pair of nodes in the network is measured by the *path length*. Collectively, the broad patterns in how nodes and edges are arranged in the network are referred to as *network topology*.

In the context of veterinary epidemiology, social network analysis has most often been used to study the spread of infectious disease through livestock trade

movements (Dubé et al., 2009; Martínez-López et al., 2009a). This is partly because movements are a significant risk factor for most economically important diseases and partly because the information stored in national cattle movement databases provides researchers with an explicit means of modelling heterogeneities in livestock contact patterns. Descriptive statistics have been published on cattle movement networks in the United Kingdom (Volkova et al., 2010; Vernon, 2011), France (Rautureau et al., 2010), Denmark (Bigras-Poulin et al., 2006; Mweu et al., 2013), Italy (Natale et al., 2009), Sweden (Nöremark et al., 2011), Spain (Martínez-López et al., 2009a), Portugal (Baptista and Nunes, 2007), and Argentina (Aznar et al., 2011). Despite significant differences in the underlying demographic structure of each industry, the resulting movement networks share many characteristic epidemiological features that have important implications for disease transmission and control.

Scale-free behaviour

Early work on human sexual contact networks first established that a small number of individuals with atypically high contact rates were disproportionately responsible for the epidemic spread of HIV as well as other sexually transmitted diseases (Gupta et al., 1989). This principle has subsequently been called the '20/80' rule to reflect the common finding across many biological systems that 20% of the host population often contributes 80% to the transmission potential of infectious pathogens (Woolhouse et al., 1997) and cattle movement networks are no exception to this rule (Woolhouse et al., 2005). The highly right skewed or *power-law* degree distribution in these networks leads the emergence of *scale-free* behaviour as described by Barabási and Albert (1999). This behaviour is characterized by the absence of epidemic thresholds in large populations (Barabási, 2009), higher basic reproduction numbers (R_0) than expected for networks with uniform degree distributions (Woolhouse et al., 2005), and greater tolerance to control measures applied to the network at random (Albert et al., 2000). The latter

provides an alternate explanation as to why voluntary disease control programmes in the cattle industry have historically made little impact on endemic disease prevalence.

From a theoretical perspective, it has been consistently shown that removing a small number of highly connected farms or movements from the network is the most cost-effective strategy for controlling disease at the industry level (Natale et al., 2009; Natale et al., 2011; Rautureau et al., 2012; Tinsley et al., 2012). Depending on the disease in question, this may be accomplished through interventions such as vaccination, diagnostic testing, quarantine, or targeted movement restrictions. Several measures are currently used to rank the relative importance or *centrality* of individual farms and individual movements in the contact network. The simplest is *degree centrality*, which measures the number of incoming and outgoing connections associated with each node. An extension of this is *neighbourhood size*, which measures the number of nodes that can be reached within a specified number of inward or outward links from a node of interest. In the literature, neighbourhood size is also referred to as *reach* (Green et al., 2009), *infection chain* (Dubé et al., 2008), *premise specific networks* (Bigras-Poulin et al., 2007), *in-* or *out- components* (Kenah and Robins, 2007b), and *k-neighbours* (Ortiz-Pelaez et al., 2006), where k refers to the number of links or distance away from the node of interest. *Betweenness centrality* measures the number of shortest paths between two nodes in the network that pass through a particular node. *Closeness centrality* measures how close a particular node is to others in the network and is calculated by taking the reciprocal of the sum of all shortest path lengths originating from or terminating at the node. *Eigenvector centrality* estimates a node's importance based on the centrality of neighbouring nodes. Care must be taken in applying eigenvector centrality to directed networks as nodes with either incoming or outgoing connections, but not both, are assigned scores of zero (Bonacich and Lloyd, 2001).

In general, removing nodes according to their centrality produces more substantial changes in transmission dynamics than removing the equivalent number of nodes at random, although it is unclear which centrality measure performs the best. In a simulation study using Italian cattle movement data, removal of 1% of nodes based on degree resulted in 88% reduction in the number of infected cases at equilibrium while removal based on eigenvector and betweenness centrality resulted in a 66% reduction in the number of infected cases (Natale et al., 2009). This is in contrast to findings from Rautureau and colleagues (2010) where the centrality measures performed equally on cattle networks and in contrast to Green and colleagues (2009) where removal of nodes from fish movement networks based on eigenvector centrality was comparable to random removal. These findings may reflect differences in network structure between livestock industries and studies as well as the benchmarks against which node removal strategies were measured.

Small-world behaviour

Another important and intuitive feature of cattle movement networks is that contacts between herds do not occur at random. Factors such as farm production type (Ezanno et al., 2006), farm disease status (Weber et al., 2006), trust between buyers and sellers (Von Bailey and Hunnicutt, 2002), access to markets (Hobbs, 1997), and distance between farms (Lindström et al., 2009) all contribute to the observed patterns of cattle movements. In particular, the significant costs associated with marketing and transporting cattle over long distances tends to result in networks with *small-world* properties, characterized by the local clustering of contacts with the occasional long distance jumps that are responsible for bridging distant network communities (Watts and Strogatz, 1998). As a disease control strategy, removing these so-called *linkage* movements increases the likelihood of epidemic extinction due to the rapid depletion of susceptible local contacts (Keeling, 1999; Newman, 2003). In a real world setting, this would involve identifying linkage movements in advance and then either preventing the contact from forming

or implementing additional biosecurity measures, such as testing or quarantine, to effectively remove it from the network.

There have been two primary methods used to identify linkage movements in contact networks. The first, *edge betweenness centrality*, measures the number of times a network edge falls on the shortest path between pairs of nodes (Girvan and Newman, 2001). The higher the betweenness centrality score, the more influence the network edge has on transmission dynamics. The second method is based on identifying community structures in contact networks and then searching for edges that bridge different communities. Although the algorithms for detecting community structure are highly diverse (Fortunato, 2010), most are based on the general concept that nodes within a community are more connected between themselves than to other nodes in the network. Grisi-Filho and colleagues (2013) recently reviewed their applications to livestock trade networks and highlighted that community detection analysis may be of additional epidemiological use for zoning trade regions or conducting risk-based surveillance.

Network topology measures

Network *density* measures the proportion of all possible connections between nodes that are observed in the network. Livestock networks are characteristically sparse, but variably so. For example, Volkova and colleagues (2010) report a network density in Scotland10 times greater than that reported by Lindström and colleagues (2009) in Sweden during the same time period using comparable network definitions, which suggests significant underlying differences in industry structure and herd management practices. A closely related measure is the network *fragmentation index*, which measures the proportion of pairs of nodes that are not connected by any path. Intuitively, pathogens can spread more readily through networks that are dense and well connected.

The *giant strongly connected component* (*GSCC*) is the largest subset of nodes that are mutually reachable via directed links. For every pair of nodes *i* and *j* in the

GSCC, if there is directed path from *i* to *j*, there implicitly must also be a directed path from *j* to *i*. Therefore, by definition, an epidemic seeded in GSCC has the potential of spreading to all other nodes in the GSCC. Consequently, this measure has been widely used to estimate the lower bounds of an epidemic (Kenah and Robins, 2007b, a). In a theoretical model of foot-and-mouth disease transmission, GSCC correlated well with final epidemic size when movements and elements of locally based transmission were incorporated (Kao et al., 2006). As a measure of overall industry connectivity, Robinson and colleagues (2007) observed that increases in the GSCC sizes for monthly cattle movement networks over a four year period may indicate growing potential for large scale epidemics. Several studies have also used GSCCs to explore the importance of individual nodes and edges in driving global network structure. Kao and colleagues (2007), for example, note that the presence of high-risk movements through livestock markets cause the GSCC to grow faster than movements occurring directly between farms. In a similar model, Rautureau and colleagues (2010) found that removing less than 1% of the most central nodes, chiefly markets and dealers, caused substantial reductions in GSCC size.

Average path length measures the average distance required to reach any given node from any other node in the network along a series of shortest paths, where the shortest path is defined as the fewest number of contacts required to reach node *i* from node *j* (Watts and Strogatz, 1998). In theoretical models of epidemic spread, average path length is positively correlated with the time taken to reach maximum epidemic size (Shirley and Rushton, 2005). The 'closer' nodes are in network distance, the faster disease can spread between them. Many real world biological and social networks are structured to minimize the effort needed to connect any two nodes (Tero et al., 2010). Highly connected nodes or *hubs*, such as livestock dealers, are instrumental in decreasing average path length (Barabasi and Albert, 1999).

The network *clustering coefficient* or *transitivity* measures the probability that any two immediate neighbours of a node are also directly connected. When disease is introduced to a highly clustered network, it tends to rapidly saturate local susceptible contacts and maximum epidemic size is reduced unless there are many links bridging local clusters (Keeling, 1999; Newman, 2003). Higher clustering coefficients have also been associated with smaller GSCC sizes. These findings are somewhat difficult to apply to livestock contact networks because the calculation implicitly ignores edge directionality and the clustering coefficients observed in livestock networks are approximately 2 to 3 orders of magnitude smaller than those tested in theoretical network models (Newman, 2001, 2003; Moslonka-Lefebvre et al., 2009; Badham and Stocker, 2010). Eubank and colleagues (2004) also suggest that while network clustering may drive short term disease spread, other global structural properties of contact networks may be more important for shaping long term dynamics.

Degree assortativity (hereafter referred to simply as assortativity) is a measurement of the likelihood that nodes will make preferential contact with other nodes of similar degree. Negative values indicate that the network is disassortative, meaning that high degree nodes make more frequent contact with low degree nodes. Positive values indicate that the network is assortative, meaning that high degree nodes make more frequent contact with other high degree nodes. Epidemics on assortative networks have faster initial growth rates and shorter durations because the high degree nodes tend to form a strongly connected component that saturates quickly (Kiss et al., 2008). Newman (2002) suggests that the giant components of assortatively mixed networks can sustain an epidemic in cases where edge density would ordinarily be insufficient to allow disease to persist and that targeting highly connected nodes in assortative networks is a less effective control strategy than for disassortative networks. In general, cattle movement networks tend to be mildly disassortative due to the scale-free degree distribution (Mweu et al., 2013).

Methodological limitations

Although network analysis has provided many valuable insights into the contact structure of cattle industries, the methodologies were originally designed for human social networks where the nodes represent individuals rather than populations and the contacts between individuals tend to be relatively more stable and persistent over time. Accounting for the unique demographic characteristics of the individual herds and the animals that move between them can greatly enhance the predictive value of network-based simulation models. The most common approach for including temporal structure into network models has been to replicate movements exactly as they occurred in the database. Model duration is either limited to the time span of the available movement data (Dubé et al., 2011) or subsets of the data are recycled to allow longer simulation runs (Carslake et al., 2011; Tinsley et al., 2012). Neither method allows the network structure to vary dynamically over time as farmers respond to the presence of disease and disease control regulations. Nor do they allow researchers to study the effects of interventions such as trade regionalization or market closure. This will require the development of network generation models that are complex enough to capture the epidemiologically important features of trade networks, yet simple enough to be computationally tractable.

Network demographics

Cattle production systems have often been described as structured metapopulations, reflecting the fact that each herd has its own unique demographic characteristics that determine the risk, severity, and duration of infectious disease outbreaks. This concept originated from the field of ecology as a framework for describing a 'population of populations' (Levins, 1969). Much is still unknown about the precise mechanisms driving the differences between herds, but factors such as herd size (Brooks-Pollock and Keeling, 2009), management structure (Ezanno et al., 2008; Marcé et al., 2011), population turnover (Ståhl et al., 2008),

biosecurity practices (Flaten et al., 2005), and geographic location (Ersbøll et al., 2010) are believed to be important. Traditional static network measures do not provide a means of weighting individual nodes according to their estimated risk, which is another reason why simulation modelling is rapidly becoming the gold standard for exploring the epidemiological properties of cattle contact networks. In this context, the within-herd transmission dynamics can either be described through simple compartmental models (Liu et al., 2007; Courcoul and Ezanno, 2010) or more complex individual-based models where real data is used to inform the demographic changes (Keeling et al., 2010; Carslake et al., 2011). Some studies have even gone as far as describing herds themselves as metapopulations and used network-based approaches to model the contacts of individual animals within production groups (Turner et al., 2008; Duncan et al., 2012).

It is also important to consider that the edges in cattle movement networks represent individuals with unique demographic characteristics rather than simply a contact between two herds. As numerous empirical studies have shown, the probability of any individual animal being infected or transmitting disease to susceptible cattle is strongly influenced by factors such as age, production type, and on-farm management practices (Daniels et al., 2002; Ohlson et al., 2010; Ramírez-Villaescusa et al., 2010; Carslake et al., 2011). This becomes particularly important when modelling the spread of specific endemic pathogens. For example, contagious mastitis is highly unlikely to spread through the movements of male cattle or store calves purchased for fattening, whereas older lactating dams are predicted to have a significantly increased risk based on the higher prevalence of disease and greater opportunity to spread disease through contaminated milking equipment (Zadoks et al., 2001; Garcia Alvarez et al., 2011). Furthermore, the sensitivity and specificity of diagnostic tests used to effectively remove the edge from the network can also vary based on the animal's demographic characteristics (de la Rua-Domenech et al., 2006; Nielsen and Toft, 2008). In this case, however, there are methods that can be

adapted from social network analysis to weight the relative risk of network edges (Newman, 2004a).

Temporal dynamics

Static network topology measures are widely reported in the literature because they can be calculated with relative computational ease. However, their utility for predicting disease transmission dynamics in cattle production systems is inherently limited by the assumptions that contacts are fixed over time. Most cattle movements occur only once without ever being repeated (Ezanno et al., 2006; Vernon, 2011) and through dynamic simulation models it has been consistently shown that accounting for the precise timing and sequence of movements can greatly influence predictions of epidemic behaviour (Dubé et al., 2008; Vernon and Keeling, 2009; Bajardi et al., 2011; Natale et al., 2011). For example, in a study of dairy cattle movements in Canada, the GSCC sizes measured over 4 week intervals provided estimates of final epidemic size that were two to three times larger than the actual number of premises reachable from a given infected node when movement dates were considered (Dubé et al., 2008). Another study tested a range of static and dynamic network representations finding that static networks overestimated the extent of disease spread, although the differences were less pronounced when the transmission probabilities were low (Vernon and Keeling, 2009).

Across many disciplines there is also growing awareness that changes in host behaviour over the course of an epidemic can significantly alter disease transmission dynamics (Funk et al., 2010). In livestock production systems, any disease intervention that imposes financial or physical barriers to trade is likely to change contact patterns as farmers develop alternate marketing strategies to reduce the impact on their business. Robinson and colleagues (2007), for example, documented a linear increase in the size of weekly GSCCs after movement standstill legislation was introduced in 2002, which suggested that mechanisms developed to maintain trade actually increased the potential for larger scale epidemics. Changes

in trade behaviour were similarly noted following the introduction of pre-and post-movement testing from regions with high incidence of bovine tuberculosis (Christley et al., 2011). Farmers were more likely to move single animals from high risk regions rather than large batches, while overall movements between farms in high risk areas had decreased. Subsequent work by Vernon and Keeling (2012) has confirmed that the protective effects of movements regulations in the UK tend to diminish over time. The authors emphasized the need to develop epidemiological models that allow network structure to vary dynamically in response to control interventions.

Network generation models

Current methods for generating contact networks are limited by their 'top down' approach, which relies on using arbitrary rules and scaling constants to replicate features observed in real networks (Hakansson et al., 2010). For example, preferential attachment has been used as a mechanism to explain scale-free degree distributions (Barabasi and Albert, 1999). In this system, the probability of a new connection forming with a node is significantly greater if the node already has other network contacts. Additional rules can be introduced to increase the likelihood that any two neighbours of a node will also form connections, thereby creating networks with specified clustering coefficients (Newman, 2001; Holme and Kim, 2002; Vazquez, 2003). However, this has little meaning for cattle movement networks where structural topology arises from decisions made by individual farmers on the optimal time and market to trade replacement cattle. Some of these decisions are based on social tradition, while others conform to logical constraints such as transportation costs, market access, and seasonal cattle inventories.

An alternative approach is to generate contact networks from first principle based on a sound understanding of the biological, social, and financial factors driving contact formation (Mahmood et al., 2010). Recent work in the human literature demonstrated that it was possible to replicate mobility patterns from

information on job opportunities and the assumption that individuals would seek to maximize income while minimizing commuting distance (Simini et al., 2012). In the cattle industry, high transportation costs also result in most contacts occurring over short distances. Lindström and colleagues (2009) used this principle to construct theoretical cattle networks where the probability of contact formation was modelled as a function distance between herds. Stochastic block modelling, where farms are assigned into groups and contacts generated based on the probability that any two farms within a group or between groups will form a contact (Karrer and Newman, 2011), was used successfully to contact networks with spatial clustering to describe transmission pathways for the 2007 equine influenza outbreak in Australia (Firestone et al., 2011). However, both approaches ignored the timing of movements and the production characteristics of the farm, which are important constraints to contact formation.

Conclusion

Endemic diseases have a significant impact on the performance and sustainability of cattle production systems. Although there have been tremendous advances in our understanding of how these diseases interact with their epidemiological environment, there is a strong need for further research into the economic and behavioural drivers of contact patterns. The detailed information on industry demographics recorded in national cattle movement databases provides a valuable foundation for these analyses.

Thesis objectives

This thesis is structured as a series of case studies that illustrate why endemic cattle diseases are difficult to control in the current epidemiological environment, how insights from network analysis can guide the development of more effective disease control programmes, and why there is a need for further research into the

underlying drivers of contact network demography. Data from the British cattle industry is used as an example.

Chapter 2 provides an introduction to the Cattle Tracing System (CTS) of Great Britain. This database contains detailed information on the movements of individual animals, which was used to reconstruct industry-level contact patterns and to generate herd-level risk factors for disease transmission. Descriptions of the bovine tuberculosis (bTB) and bovine viral diarrhoea virus (BVDV) datasets are also provided.

Chapters 3, 4, and 5 illustrate three key challenges in the current approaches to controlling endemic cattle diseases at the industry level. Chapter 3 uses surveillance data on bTB in Scotland to highlight the potential for endemic diseases to spread silently between herds due the low sensitivity and specificity of routine surveillance measures. Chapter 4 uses survey data from two national BVDV studies to show that spread through local transmission mechanisms and poor farmer compliance may reduce the efficacy of disease control programmes that strictly target cattle movements. The same dataset is used in Chapter 5 to provide evidence that the effects of endemic disease on herd performance are highly variable and may lead to misconceptions about the herd's true disease status.

Chapters 6 and 7 explore two different strategies for controlling the spread of endemic disease through cattle movement networks without the use of disease specific interventions such as testing or vaccination. In Chapter 6, it is shown that improving herd reproductive performance can lead to substantial reductions in endemic disease prevalence by eliminating extraneous replacement breeding cattle movements (a 'bottom up' approach'). In Chapter 7, it is shown that selectively restricting the choice of network contacts can alter disease transmission dynamics while still allowing farmers to trade the required number of cattle (a 'top down' approach)..

Chapters 8 and 9 provide quantitative evidence of the need for further research into the demographic and behavioural drivers of contact network structure.

Chapter 8 challenges the current network based approaches to modelling endemic disease transmission by showing that the risk of cattle movements causing disease outbreaks is strongly influenced by the demographic characteristics of the purchased animal and the receiving herd. In Chapter 9, it is shown that the introduction of mandatory post-movement testing for bTB had the unintended and epidemiologically advantageous effect of reducing high risk cattle imports into Scotland.

Chapter 10 finishes with a critical assessment of how the data and modelling approaches used in this thesis can support the development of more sophisticated epidemiological models in the future.

Chapter 2

Cattle movement and disease data

Cattle Tracing System data

Livestock traceability legislation

Cattle keepers in the United Kingdom have been required to individually identify animals since 1953 as part of national bovine tuberculosis control efforts. This legislation was extended in 1960 with the Movement of Animals (Records) Order, which required that records of all cattle movements on and off the premises be stored in the farm register for at least 3 years. In response to growing concerns over BSE, the Bovine Animals (Identification, Marking, and Breeding Records) Order was introduced in 1990 to ensure that the birth of calves and the identity of their dams were recorded within 36 hours of birth for dairy cattle and 7 days of birth for all other cattle. The Movement of Animals (Records) Amendment Order of 1990 extended the length of time farmers were required to maintain records on farm to 10 years. To comply with Council Directive 92/102/EEC issued by the European Economic Community (EEC) in 1992, the Bovine Animals (Records, Identification and Movement) Order of 1995 was introduced, which required all farmers to register their holding with the local Animal Health Office and all cattle to be issued a unique ear tag number of no more than 14 characters

In response to the BSE crisis, a cattle passport scheme was introduced in July 1996. Farmers were subsequently required to register the date of birth, sex, breed, and parentage of each calf born on the farm so that a physical passport could be issued by the local agricultural office. After a 2 year trial period, the cattle passport scheme was incorporated into the British Cattle Movement Service (BCMS) in September 1998. This also led to the establishment of the electronic Cattle Tracing System (CTS) database to manage the large volume of cattle records. Initial efforts were made to back-capture passport information on animals that were alive, but not

yet registered in the database with the Cattle Count exercise of 2000. Farmers have been required to report all births, deaths, and movements of cattle to BCMS since January 2001, which has greatly improved the quality of movement records stored in CTS database (Mitchell et al., 2005; Green and Kao, 2007). Extracts of the CTS database are provided to researchers through the Rapid Analysis and Detection of Animal-related Risks (RADAR) project. This initiative was started by the Department of Environment, Food, and Rural Affairs (DEFRA) in 2005 to collect veterinary surveillance data from different sources.

Movement control legislation

In response to the 2001 FMD outbreak, the UK government introduced movement standstill regulations increase the likelihood of detecting FMD introduced to a farm through recent movements before potentially infectious animals were next shipped off the premises. Initially, the movement of any cattle, sheep, goats, pigs, or deer onto a premise triggered a 20 day standstill in movements off the premises based on the perceived maximum time that FMD could incubate in a herd before detection. It was subsequently reduced to six days for all livestock species except pigs by the Disease Control (England) Order of 2003. Movements to slaughterhouse either directly from the farm or indirectly through market are exempt from the herd standstills. No direct movements from market to market are permitted. Scotland maintains different regulations under the Disease Control (Interim Measures) (Scotland) Order first introduced in February 2002. The standstill for all livestock species except pigs is 13 days and a number of additional exemptions exist for the movement of animals from premises to shows, exhibitions, artificial insemination centres, and veterinary treatment facilities.

Farm registration

All agricultural holdings in the United Kingdom that house cattle, sheep, goats, and pigs must be issued a unique County Parish Holding (CPH) number to report livestock movements and to apply for agricultural subsidy payments. This

includes locations classified as farms, auction markets, calf collection centres, dealers, veterinary practices, abattoirs, common grazing land, and other holding facilities. The CPH number includes a 2 digit county code, a 3 digit parish code, and a 4 digit holding number in the following format: CC / PPP / HHHH. The current regulations for cattle keepers allow all fields and buildings within a 10 mile radius of the main farm site to be registered under a single CPH number. Temporary CPH numbers (identified by a holding number in the 7000 range) may be issued to landless keepers who raise livestock on rented land and to farmers who wish to register seasonal grazing pastures separately from the main farm CPH number for subsidization purposes. Farmers who rent land from another livestock keeper may also apply for a temporary CPH number to prevent movements onto the main farm holding from triggering standstills on the rented land. The CPH numbers assigned to individual locations over time may change through the conversion of land to cattle farming or other agricultural purposes, the transfer of an existing cattle herd to new ownership, or the creation of single holding by merging multiple land parcels.

Farms that manage cattle on multiple uniquely identified land parcels can apply for a 'linked' premises status in CTS to reduce the burden of movement reporting. Linked premises may include parcels of grazing land that fall outside the 10 mile radius or farms that share facilities such as milking parlours. Farmers are still required to maintain a permanent record of the cattle movements in the farm register, but do not have to report the movement centrally to BCMS. Discrepancies in an individual animal's life history may therefore arise, for example, if it was born on the main farm location, moved to a linked premise for fattening, and then moved off the linked premise to slaughter. In cases where the linked premises also form a single epidemiological unit, farmers can apply for Sole Occupancy Authority (SOA) status, which allows animals to move between premises in the SOA without triggering a movement standstill.

Movement recording

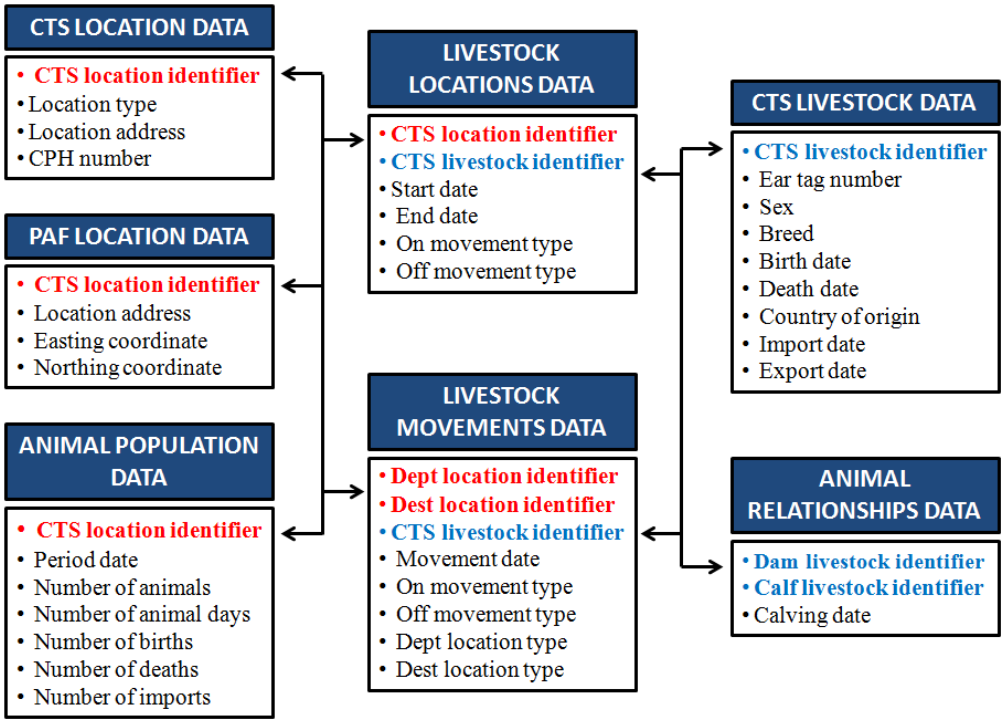
Every newborn calf in the United Kingdom is required to have an ear tag fitted in both ears with the country code, herd mark, and individual animal number. Dairy farmers must fit the ear tag within 36 hours of birth, while beef farmers have up to 20 days. Farmers are required to apply for a cattle passport within 27 days of the calf being born or within 7 days of tagging and must provide information on the animal's breed, sex, genetic dam, and date of birth. Cattle that are imported to the United Kingdom must also be issued a passport unless they are to be slaughtered within 15 days. Farmers are not required to report the birth of stillborn calves or calves that die before being tagged, although records of these animals must be kept on farm. For tagged animals that die on farm, the death must be reported and the passport returned to BCMS within 7 days.

A cattle movement is defined as the movement of a live animal 'on' or 'off' a holding. This includes private sale and movements to or from markets (even if the animal is not sold), slaughterhouses, showgrounds, and separately managed, but unlinked holdings. Both the sender and receiver of cattle are required to report the movement within 3 days of occurrence to improve the chances of capturing the movement correctly in the database. Under certain circumstances, the slaughterhouse may record the off movement for the sending farm. Farms may be periodically inspected and audited to ensure that animal identification and record-keeping is accurate.

Database structure

The CTS database contains seven primary data tables that provide detailed information on the movements and demographic characteristics of individual animals and livestock locations. A schematic representation of the database structure is shown in Figure 2.1. The extract used in this thesis contained all known records through April 2010.

Figure 2.1: Schematic representation of the Cattle Tracing System database structure and relationships between data tables.



There are three data tables that describe the locations on which cattle may be held. The CTS location data table contains information on the location type (agricultural holding, landless keeper, market, showground, slaughterhouse, and other location types), the location address (business name, street address, town, county, and postcode), and the unique CPH number. For locations that belong to a larger farm business, the address details may be for the main farm business rather than the actual location where cattle are kept. For slaughterhouses, the CPH number may be replaced by the official 4-digit EEC abattoir code. This table provides the primary means of linking farm data from other national animal health databases or survey studies with the CTS movement records. The Postal Address File (PAF) location data table provides an easting and northing coordinate for approximately 65% of locations listed in the CTS database (Mitchell et al., 2005). This information is the result of georeferencing the address details from the CTS database. The

Animal population data table provides summary statistics on the number of animals, animal days, births, deaths, and import movements associated with each location in a given calendar month. This information can be used to identify whether a location housed cattle at any given time point and to distinguish breeding herds from fattening herds.

There are two data tables that describe the movement and location history of individual cattle. Both are derived from the unpaired on and off movement records supplied to BCMS by cattle keepers. The Livestock locations data table is a list of stays of animals on locations and each observation contains information on the identity of the animal and location, the date of arrival and departure, and the type of arrival and departure (birth, movement, or death). This table can be used to identify cattle that were present on any given location on any given date. The Livestock movements data table is a list of the paired on and off movements used to identify transfers of cattle between livestock locations. Each observation contains information on the identity of the animal, the identity and location type of departure and destination location, the movement date, and the type of movement (birth, movement, or death). This table provides the basic information needed to reconstruct the cattle movement network.

The final two tables contain the demographic information recorded in each animal's passport. The Livestock data table records the animal's sex, breed, ear tag number, birth date, death date (if applicable), country of origin (if imported from overseas), and import and export dates (if applicable). Animals that were entered into the CTS database retrospectively are frequently missing a birth date. The Livestock relationships data table provides a link between the dam and calf identification numbers, which can be used to generate a list of calving events for each dam. The information from these two tables can be linked with the movement and location records to deduce the animal's production purpose at any given time point.

Bovine tuberculosis data

Routine surveillance measures

A compulsory surveillance programme for bovine tuberculosis (bTB) has been implemented in Great Britain since the 1950s. The current guidelines stipulate that every herd should be routinely tested for bTB using the single intradermal comparative cervical tuberculin (SICCT) test at intervals from 1 to 4 years depending on the perceived herd-level risk. Herds in agricultural parishes where the prevalence of bTB is high are tested at 1-year intervals and, in general, all animals over 42 days of age are tested. In Scotland, routine testing is normally conducted once every 4 years and includes all female cattle that have previously calved, bulls greater than 12 months old unless exempted by a veterinarian, any cattle greater than 6 weeks old which could be used for breeding, and any cattle purchased since the last herd test. A small number of herds considered to be at increased risk of acquiring and transmitting bTB, including herds with regular intake of cattle from the Republic of Ireland or Northern Ireland, herd that retail raw milk, and newly formed herds are subject to a greater frequency and intensity of testing.

The carcasses of all individual cattle that are slaughtered at registered abattoirs in Great Britain are also subject to examination for lesions consistent with bTB as part of routine food safety inspections. However, it has been estimated that standard food safety inspections at abattoirs miss up to 47% of cattle with visible tuberculosis lesions (Corner et al., 1990).

The post-movement testing of cattle over 42 days of age imported to Scotland from herds in England and Wales subject to annual herd testing was first required in September 2005. All post-movement tests must be carried out within 60 to 120 days of the animal arriving on the receiving Scottish farm, unless the animal is slaughtered during that time period. This legislation was expanded in February 2010 to require post-movement testing for all animals imported into Scotland from

England and Wales regardless of the bTB testing interval with the exception of those shown to have spent their entire lives in low incidence region. Complementary pre-movement testing of cattle moved from herds in England and Wales subject to annual herd testing was introduced in May 2006. Animals must be tested within 60 days of moving off the farm unless the animal is moved directly to slaughter, to and from an exempt agricultural show, moved within a SOA, moved between premises sharing rights of the same common, or moved to and from a facility for veterinary treatment, Cattle imported to Great Britain from the Republic of Ireland and Northern Ireland must also be post-movement tested between 60 and 120 days of arriving in a Scottish herd. Herd owners are responsible for the costs of pre- and post-movement testing, although routine herd tests paid for by the government during the specified time windows can be substituted for pre- or post-movement tests.

Test interpretation

The SICCT used for both routine herd testing and movement-associated testing compares the sensitivity of individual cattle to bovine and avian mycobacterial antigens injected intradermally at separate sites on the neck. Depending on the relative degree of reaction to the antigens after 72 hours and the perceived herd-level risk for bTB, animals may be classified as positive reactors, inconclusive reactors, or negatives (Green and Cornell, 2005). The sensitivity of SICCT for detecting infected cattle ranges from 68% to 99% and the specificity ranges from 79% to 99% (de la Rua-Domenech et al., 2006; Clegg et al., 2011). For that reason, herds with positive reactors are only considered confirmed "breakdowns" if either visible pathognomonic lesions of infection with *Mycobacterium bovis* are observed during *post-mortem* examination of positive reactors or *M. bovis* is cultured from tissue samples. Cattle with an inconclusive SICCT may be re-tested up to two times or slaughtered to examine for visible lesions. The sensitivity of *post-mortem* examination for identifying cattle with

visible lesions ranges from 86% to 95% (Byrne, 1992; Corner, 1994; Whipple et al., 1996; Norby et al., 2004).

At the herd level, detection of a confirmed reactor through routine herd testing or of a lesioned carcass at slaughter inspection triggers immediate animal-movement restrictions, testing of all cattle at 60 day intervals until no further reactors are disclosed, testing of contiguous herds within a 3 km radius of the confirmed positive herd, and testing of herds that can be linked to the confirmed positive herd through animal movements. In some cases, the presence of unconfirmed positive or inconclusive reactors may also trigger follow-up testing if there is reason to suspect bTB in the herd, *e.g.* a known movement of cattle from a herd infected with bTB.

VETNET database

Results of all *ante-mortem* bTB tests in Great Britain and information on suspected and confirmed cases identified through slaughter surveillance have been collated in the VETNET database maintained by the Department for Environment, Food and Rural Affairs (DEFRA) since the 1990s. Negative results for a herd test are reported *en masse* with the following summary information: number of cattle tested, total number of animals in the herd, date and type of test, herd production type, and administrative information for the farm including the county-parish-holding (CPH) identifier of the main farm business, the farm address, and the farm coordinates. When a positive or inconclusive reactor is identified, the passport number of the animal is entered along with any follow-up test results or actions taken. For herds with multiple reactors, the information on whether lesions were observed at *post-mortem* examination or positive cultures for *M. bovis* were obtained from tissue samples is aggregated at the herd level and it is therefore not possible to distinguish which individuals were confirmed positive.

Bovine viral diarrhoea virus data

Two national studies were conducted between October 2006 and May 2008 to estimate the seroprevalence of BVDV amongst herds in the Scottish beef suckler and dairy industries (Brülisauer et al., 2010; Humphry et al., 2012). The beef suckler study was a cross-sectional survey of 552 herds selected from a random sampling frame of holdings with at least 20 mature female breeding cattle reported in the 2004 agricultural census. Of these, 301 farms were eligible and agreed to participate in the study. During the farm visit, blood samples were taken from approximately 10 randomly selected cattle between 6 and 16 months of age and processed using an indirect BVDV antibody ELISA to obtain antibody titres on each individual. Animals under 6 months of age were not sampled because the presence of maternal antibodies can interfere with test interpretation (Palfi et al., 1993). The percentage positivity scores for each animal were calculated by dividing the optical density of the individual samples by the optical density of the positive reference sample. Animals with a percentage positivity score of greater than 14% were considered seropositive.

Spot test sampling of sentinel groups is considered a cost-effective means of detecting herds that are most likely to contain persistently infected cattle (Houe et al., 2006). However, as a study from dairy herds in Denmark illustrated, only 27% of herds in which at least 8 out of 10 sampled young stock were antibody positive for BVDV were subsequently found to contain PI animals when the entire herd was sampled (Houe, 1994). Similar issues with specificity are also likely to be present for beef suckler herds. Based on statistical criteria previously described for these data (Brülisauer et al., 2010), the 225 herds with no serological evidence of active infection in young stock were considered control herds and the remaining 76 herds with a within-group prevalence of more than 26.3% were considered seropositive case herds. Farmers were also administered a questionnaire at the time of sampling

(Appendix A) to obtain information on herd demographic structure and management practices that may be associated with BVDV seropositivity.

The dairy study aimed to collect bulk milk tank samples from as many Scottish herds with at least 30 mature female breeding cattle as possible. All major milk purchasers in Scotland were initially contacted and asked to take samples from farms during routine milk collection. Farmers were also provided with a management questionnaire (Appendix B) at the time of sampling to be returned voluntarily to the Scottish Agricultural College. A total of 374 farms out of approximately 1,345 eligible farms in Scotland participated in the study. However, the final sample was restricted to the 220 herds that did not routinely vaccinate for BVDV as the presence of vaccinal antibodies can interfere with test interpretation (Houe et al., 2006).

The bulk milk tank samples were processed using an indirect BVDV antibody ELISA to obtain the percentage positivity scores. It is has previously been shown that there is a strong relationship between the level of antibodies in bulk tank milk and the percentage of cows in the milking herd that are antibody positive on serology (Beadeau et al., 2001; Niskanan, 1993). The sensitivity and specificity of bulk milk tank ELISA in detecting herds with likely BVDV infection has been estimated at 81% and 91%, respectively (Thobokwe et al., 2004). However, a study from Northern Ireland showed that only 5 of 49 dairy herds with high bulk milk tank antibody levels had detectable virus in the milk (Graham et al., 2001).

In this thesis, the class system used in the Swedish BVDV eradication programme was used to assign the 220 unvaccinated herds into one of four groups based on their percentage positivity score (Alenius et al., 1997). The scores ranged from Class 0 herds, considered unlikely to include any seropositive animals and indicating a low probability of BVDV infection, to Class 3 herds, considered highly likely to have many seropositive animals indicating a recent or active infection. For the purpose of this analysis, the 77 herds designated as Class 0 or Class 1 were

considered control herds and the remaining 143 herds designated as Class 2 or Class 3 were considered seropositive case herds.

Full details of the survey designs and methodological limitations can be found in (Brülisauer et al., 2010) for the beef suckler study and (Humphry et al., 2012) for the dairy study. These sampled herds were previously shown to be well representative of the population of Scottish beef and dairy herds.

Chapter 3

Risk factors for bovine tuberculosis in low incidence regions related to cattle movements

Summary

Bovine tuberculosis (bTB) remains difficult to eradicate from low incidence regions due to the limited sensitivity and specificity of routine surveillance methods. In this analysis, data from Scotland in the period leading to Officially Tuberculosis Free (OTF) recognition were analyzed retrospectively for evidence of disease transmission in the delay between introduction through cattle import movements and detection through routine herd testing or slaughter inspection. From 2002 to 2009, approximately 75% of new confirmed breakdowns were detected through cattle with no known movements outside Scotland, which suggests that on-farm transmission takes place. At the animal level, cattle that were purchased from Scottish herds with confirmed reactors and recent import movements had 2.99 times greater odds (95% CI: 1.31 – 6.76, p = 0.009) of being identified as reactors than cattle purchased from other Scottish herds, while cattle purchased from Scottish herds with unconfirmed reactors and recent import movements were at 1.63 times greater risk (95% CI: 1.14 – 2.33, p = 0.008). Similar findings from the herd-level risk factor analyses support the hypothesis that many of these unconfirmed herds were truly infected with bTB and a potential risk to other herds through animal movements. However, case-control comparisons revealed that the number of cattle tested, the presence of imported cattle, the test status of neighbouring herds, the geographic location within Scotland, and the presence of poultry may interfere with the interpretation of routine herd tuberculin tests. For low incidence regions, targeted pre- and post-movement testing of imported cattle appears to be the most effective surveillance strategy for reducing the incidence of confirmed and unconfirmed bTB breakdowns.

Introduction

The control of bovine tuberculosis (bTB) in domestic cattle herds remains an ongoing and costly challenge for many industrialized countries, including those that have achieved tuberculosis free status (Cousins and Roberts, 2001; Schiller et al., 2011). Tuberculosis free status does not imply the complete absence of bTB, but is instead awarded to a territory where the incidence of new herd breakdowns has remained below a set threshold for a number of consecutive years and appropriate surveillance systems are in place to detect any increase in disease frequency. As the majority of infected cattle show no clinical signs, surveillance systems are generally based on *ante-mortem* testing of individual cattle using intradermal tuberculin tests at intervals determined by the herd-level risk and *post-mortem* examination of all bovine carcasses at abattoirs for lesions consistent with bTB (Cousins and Roberts, 2001; Pavlik, 2006; Radunz, 2006).

Both surveillance methods are considered good herd-level screening tools in regions where the prevalence of infected cattle in breakdown herds is generally high (Doherr and Audige, 2001). However, limitations in their sensitivity and specificity have been highlighted as the main barrier to eradicating disease from low incidence regions (Gordejo and Verneersch, 2006). The single intradermal comparative cervical tuberculin test (SICCT) used in routine herd surveillance compares the sensitivity of individual cattle to bovine (*Mycobacterium bovis*) and avian (*Mycobacterium avium*) mycobacterial antigens injected intradermally at separate sites on the neck. Depending on the relative degree of reaction to the antigens after 72 hours, animals may be classified as positive reactors, inconclusive reactors, or non-reactors (Green and Cornell, 2005). The sensitivity for detecting infected individuals ranges from 68% to 99%, but may be lower for cattle in the early stages of infection or cattle experiencing physiological stress from pregnancy, concurrent illnesses, or poor management conditions (Costello et al., 1997; de la Rua-Domenech et al., 2006; Clegg et al., 2011).

Given that the specificity of SICCT is only 79% to 99% (de la Rua-Domenech et al., 2006), most animals with positive skin reactions are slaughtered in order to confirm the presence of bTB through observation of visible lesions or isolation of *M. bovis* from cultured tissue samples. Animals with inconclusive skin reactions may be retested up to three times at two month intervals to monitor changes in the degree of reactivity. In the majority of cases, no further evidence of bTB infection is found and regulatory officials are faced with the challenge of deciding whether these herds were truly infected with bTB and should be subject to the same local disease eradication measures as confirmed breakdowns (Byrne, 1992; Goodchild and Clifton-Hadley, 2001; Norby et al., 2004). Higher false positive rates for tuberculin tests have been reported in cattle exposed to cross-reacting mycobacterial antigens in the production environment and cattle that have non-specific immunological responses to the injection itself (de la Rua-Domenech et al., 2006).

With the difficulty in interpreting both positive and negative SICCT results in low incidence regions, many tuberculosis free countries have found it more cost-effective to scale back routine herd testing programs in favour of targeted surveillance against cattle imported from endemic regions (Cousins and Roberts, 2001; Pavlik, 2006; Radunz, 2006). This approach has likely been effective in reducing the number of infected cattle entering low incidence regions due to the direct effects of testing on identifying infected cattle as well as the deterrent effects of testing on farmers' decisions to purchase cattle from endemic regions (Gates et al., 2013). However, these benefits may be partially offset by the opportunity for false negative cattle to spread disease in the delay between importation and the possibility of detection through routine surveillance, especially for countries that rely on slaughter inspection alone to identify infected cattle (Barlow et al., 1997; Fischer et al., 2005). It has been estimated that standard food safety inspections at abattoirs miss up to 47% of cattle with visible tuberculosis lesions (Corner et al., 1990).

Using data from Scottish cattle herds in the period from 2002 to 2009 leading up to Officially Tuberculosis Free (OTF) recognition, this study examined the potential for bTB to spread within and between herds due to limitations in routine surveillance methods. Particular emphasis was placed on identifying the origins of cattle disclosed as positive reactors through routine herd testing or found to have visible lesions on slaughter inspection, and estimating the risks associated with the herd's test status and import history of Scottish source herds. Case-case and case-control comparisons were also used to identify factors that may influence test interpretation.

Methods

Surveillance for bTB in Scotland

Scotland was awarded OTF status in September 2009 under the provisions of the European Union Council Directive 64/432/EEC, which require that the incidence of new herd breakdowns has remained below 0.1% for at least 6 consecutive years and appropriate surveillance systems are in place to detect newly infected herds. In the period from2002 to 2009 leading up to OTF recognition, Scotland conducted surveillance through (1) routine herd testing (RHT) using the SICCT; *(*2) *post-mortem* examination of all bovine carcasses at slaughter for visible lesions consistent with bTB; and (3) post-movement testing of cattle imported from regions of England and Wales with high bTB incidence determined by the frequency of RHT in parish of origin.

RHT in a herd is usually conducted once every 4 years and includes all female cattle that have previously calved, bulls greater than 12 months of age unless exempted by a veterinarian, cattle greater than 6 weeks of age that may be used for breeding, and any cattle purchased since the last RHT. A small number of farms considered to be at increased risk of bTB, including those with regular intake of Irish cattle, are subject to annual testing. Cattle imported from the Republic of Ireland or Northern Ireland were subject to post-movement testing throughout the study period.

Post-movement testing for cattle imported from high incidence parishes of England and Wales was first introduced in September 2005. All post-movement tests must be carried out within 60 to 120 days of the animal arriving on the receiving Scottish farm, unless the animal is slaughtered or subject to RHT during that time period. Complementary pre-movement testing was introduced in May 2006.

Cattle that react positively to SICCT on either RHT or post-movement testing are slaughtered to check for visible lesions and to collect tissue samples for bacteriological culture. At the herd level, detection of a confirmed reactor through RHT or of a lesioned carcass during slaughter inspection triggers immediate animal-movement restrictions, testing of all cattle at 60 day intervals until no further reactors are disclosed, and testing of contiguous herds within a 3 km radius of the breakdown herd or trace-linked to the breakdown herd through animal movements. In some cases, the presence of unconfirmed reactors may also trigger follow-up testing if there is reason to suspect bTB, *e.g.* a known movement of cattle from a herd infected with bTB.

Surveillance data

The results from all *ante-mortem* bTB tests and all suspected or confirmed cases identified through slaughter surveillance were collated in the VETNET database operated by the UK Animal Health and Veterinary Laboratories Agency (AHVLA). Negative results for a herd were usually reported *en masse* with summary information on the number of cattle tested, total number of animals in the herd, date and type of test, herd production type, and administrative information for the farm including its unique county-parish-holding (CPH) identifier and geographic coordinates. In cases where a positive reactor, inconclusive reactor, or lesioned animal was identified, the animal's passport number was entered in the VETNET database along with any follow-up test results or actions taken. For herds with multiple reactors, information on whether visible lesions were observed at *post-*

mortem examination or *M. bovis* was cultured from individual reactors was aggregated at the herd level.

An extract of the VETNET database containing all bTB surveillance records for Scottish cattle herds from 01 January 2002 to 31 December 2009 was obtained from the Animal Health branch of the UK Department for Environment, Food and Rural Affairs (DEFRA). This analysis focused on the subset of 12,248 beef, beef fattening, beef suckler, and dairy herds with at least one recorded RHT observation and/or a breakdown detected through slaughter inspection during the study time period. The RHT results from herds where testing was staggered across multiple dates for logistical reasons were aggregated into a single RHT observation for the calendar year preserving the median testing date for negative herds and the date where the first reactor or inconclusive reactor was identified for positive herds.

Each RHT observation was classified into one of three groups based on the aggregate test results: (1) confirmed RHT observations where at least one SICCT reactor or inconclusive reactor was identified at RHT and subsequently confirmed to have bTB through visible lesions at *post-mortem* or culturing *M. bovis* or, (2) unconfirmed RHT observations where at least one SICCT reactor or inconclusive reactor was identified at RHT, but never confirmed to have bTB by observation of lesions or positive culture, and (3) negative RHT observations where no cattle reacted to SICCT. The unconfirmed RHT category included herds that triggered precautionary local eradication measures and herds where no further action was taken. The passport numbers for all cattle identified as reactors or inconclusive reactors on RHTs and all cattle with lesions identified through slaughter inspection were recorded.

Cattle movement data

Records from the Cattle Tracing System (CTS) database were used to trace the movement history of individual cattle present in the study herds prior to the date of RHT or slaughter inspection. The age, sex, and breed classification of each

animal were recorded. Locations within Great Britain, but outside of Scotland, were classified into risk groups based on the frequency of RHT for cattle farms within the parish. A high incidence region of England or Wales was taken to be one where the parish testing interval (PTI) was 12 or 24 months and a low incidence region of England or Wales was taken to be one where the PTI was 36 or 48 months. The list of PTIs published by DEFRA in 2007 was used to determine the location risk. Imports from the Republic of Ireland, Northern Ireland, and other overseas locations were grouped together under overseas imports.

Farms inside Scotland were classified into risk groups based on their RHT or slaughter surveillance status (confirmed, unconfirmed, and negative) and import movement history (presence of imported cattle and no recent imports) at the time when studied cattle were located in the herd. Due to the infrequency of testing, all herds with confirmed and unconfirmed testing results were assumed to be at risk for spreading bTB in the 4 year period immediately before and the 4 year period immediately after testing.

The CTS database was also used to generate a list of farm locations (agricultural holdings and landless keepers) that housed cattle for at least one day between January 2002 and December 2009. Easting (increasing from west to east) and northing (increasing from south to north) coordinates within Great Britain for the locations were obtained from either the VETNET database or the CTS's Postal Address File. This information was used to calculate the total number of farms within a 5 km radius of each study herd and, through linking with the remainder of VETNET data, whether at least one of those farms had a confirmed breakdown identified through any surveillance branch or unconfirmed reactors identified through RHT.

The total number of individual cattle present in Scotland and the total number of animals from Scottish farm locations slaughtered at abattoir in Great Britain from 2002 to 2009 were also recorded to provide descriptive statistics on surveillance coverage.

Agricultural census data

Data from the annual June Agricultural Census of Scottish agricultural holdings provided by the Scottish Government were used to determine the average numbers of sheep and poultry present on the study farms in any given year from 2002 to 2009. The purpose was to explore whether these livestock species may be serving as potential reservoirs of *M. bovis* or other cross-reacting mycobacterial antigens that may lead to false positive RHT results.

Data quality issues

The VETNET, CTS, and June Agricultural Census databases each have different standards for recording information on individual cattle and herds. A number of observations were excluded from the analysis because the cattle passport number or the farm CPH code recorded in the VETNET database could not be linked to records in the CTS or Census databases. This primarily affected herds where cattle are housed on separate locations from the main farm building. Descriptive statistics on the data linkage efficiency for individual reactors and individual herds by case type are presented in Table 3.1.

Table 3.1: Descriptive statistics on losses due to database linkage errors.

	Animals		Herds			
Database		**CTS**		**CTS**	**Census**	**Both**
	Total	**Matched**	**Total**	**Matched**	**Matched**	**Matched**
Case type						
Slaughter case	61	54	49	46	44	44
Confirmed RHT	118	112	61	61	59	59
Unconfirmed RHT	1609	1,523	968	966	910	904
Negative RHT	-	-	11170	11152	10061	9969
Total	**1788**	**1689**	**12248**	**12225**	**11075**	**10976**

Statistical analyses

A series of four statistical analyses was performed to evaluate the effects of routine surveillance design and cattle movements on the risk of disclosing reactors through RHT or lesioned cattle through slaughter inspection.

The first analysis explored changes in the risk of farms with recent import movements and farms with no recent import movements disclosing at least one reactor on RHT or lesioned animal on slaughter inspection over time from 2002 to 2009. Recent import movements were defined as purchasing at least one animal from overseas or from high incidence parishes of England and Wales during the 4 year period prior to the testing or inspection date. Two univariate logistic regression analyses were performed using test year as the categorical independent variable and 2002 as the reference year. In total, there were 565 observations with reactors and recent import movements in the first case group, 546 observations with reactors and no recent import movements in the second case group, and 22,983 RHT observations used as controls for both case groups. To correct for herds with multiple test observations over the 8 year period, herd was included as a random effect in the model.

The second analysis explored the animal-level risks of being identified as a reactor on RHT or lesioned animal at slaughter associated with the prior movement history. The movement history of all cattle present in the confirmed and unconfirmed herds on the RHT or on the positive slaughter inspection date was traced. Due to the left censoring bias in the available surveillance data and movement data, this analysis was restricted to data from 2006 to 2009. It was also restricted to cattle that were located on at least one other farm prior to the farm of testing/inspection to reduce biases associated with the selection criteria for animals to be tested with RHT. The final sample contained 376 animals identified as reactors or lesioned cattle and 36,176 control animals. A series of eight binary categorical movement variables were created to describe the herd's movement history, including movements from (1) overseas, (2) high incidences parishes of

England and Wales, (3) confirmed Scottish herds with imported cattle, (4) confirmed Scottish herds with no imported cattle, (5) unconfirmed Scottish herds with imported cattle, (6) unconfirmed Scottish herds with no imported cattle, (7) negative Scottish herds with imported cattle, and (8) negative Scottish herds with no imported cattle. The variables were screened individually used 8 total mixed-effect multivariate logistic regression models. The farm CPH code was included as a random effect to account for variation between herds. Age and sex were included as independent variables in all models as these are potential confounders for being identified as a reactor on RHT.

The third analysis explored the herd-level risk factors for having at least one reactor on RHT or lesioned animal on slaughter inspection based on the history of cattle moved onto the farm in the 4 year period prior to testing. The analysis was again restricted to data from 2006 to 2009 to account for the left censoring bias in the cattle movement data. For herds with multiple RHTs during this time period, a single observation was selected at random so that each herd appeared only once in the analysis. The resulting sample contained 396 case herds and 9,088 control herds. The same eight binary movement variables were screened using multivariate logistic regression models with the total number of cattle moved on included in all models as as a potential confounder

The fourth analysis used a case-case comparison between confirmed and unconfirmed RHT herds and a case-control comparison between unconfirmed and negative RHT herds to identify demographic risk factors that may increase the risk of disclosing reactors on RHT. All data from 2002 to 2009 was included and the independent variables were (1) total number of animals present in the herd, (2) percentage of imported animals in the herd, (3) total number of cattle tested, (4) total number of cattle moved onto the farm, (5) total number of farms within a 5 km radius, (6) test status of neighbouring farms within a 5 km radius, (7) easting coordinate, (8) northing coordinate, (9) herd type, (10) average number of sheep present on the farm, and (11) average number of poultry present on the farm over the

8 year period. Variables 1, 3, 4, 5, 10, and 11 were log transformed prior to analysis. Variables 7 and 8 were expressed in units of 100 km. After excluding farms with missing data, there were 59 herds with confirmed RHT or slaughter breakdowns, 904 herds with unconfirmed reactors on RHT, and 9,969 herds with negative RHTs only from 2002 to 2009.

Preliminary univariate logistic regression analyses were performed to select variables with a p-value < 0.20 for inclusion in the multivariate logistic regression models. Components of the final multivariate models were determined by a backwards stepwise elimination process in which variables with the highest p-values were sequentially removed in turn until all the remaining variables in the model had a p-value < 0.05. Forwards stepwise selection was then performed adding in each of the eliminated variables in turn and checking for p-values of < 0.05 to ensure that none of the variables were excluded based on the order of elimination.

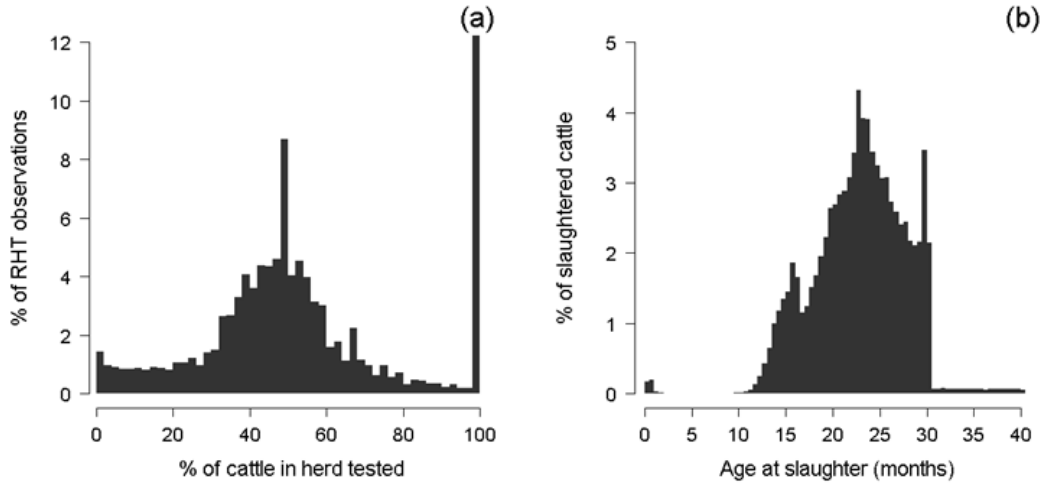
For all logistic regression models, the odds ratio (OR) and 95% confidence intervals (CIs) of the independent variables significantly associated with the outcome were reported. Associations with a p-value < 0.05 were considered statistically significant. The cattle movement data was extracted from the CTS database using the Python programming language and all statistical analyses were performed in R (R-Development-Core-Team, 2010).

Results

An estimated 7.25 million individual cattle were located on Scottish farms between January 2002 and December 2009 with an average of 1.92 million cattle present on any given date. During this time period, 4.36 million (60.1%) cattle were subject to *post-mortem* examination at abattoir and 1.68 million individual SICCTs were performed with approximately 21% of all active cattle farms subject to RHT in a given year. As shown in Figure 3.1, there was wide variation in the percentage of

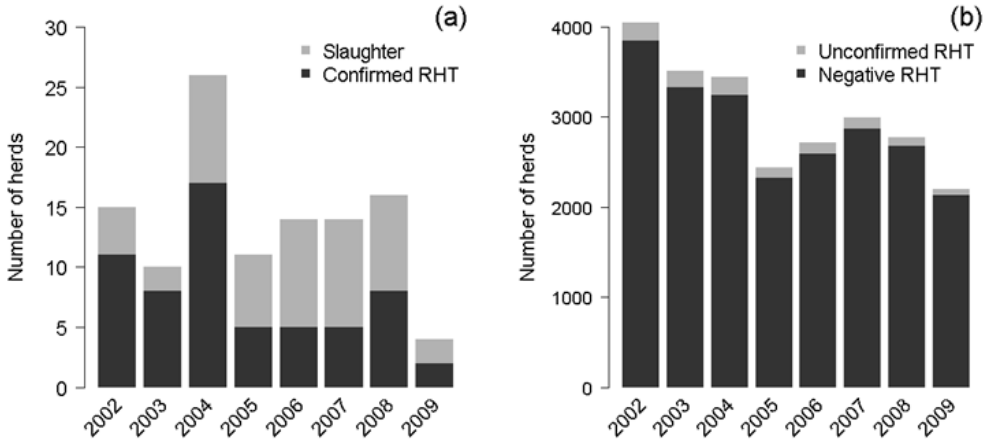
cattle in each herd that were tested during a single RHT and over 85% of cattle were less than 30 months of age when slaughtered at abattoir.

Figure 3.1: (a) Percentage of cattle tested during a single RHT observation and (b) age of cattle at slaughter.



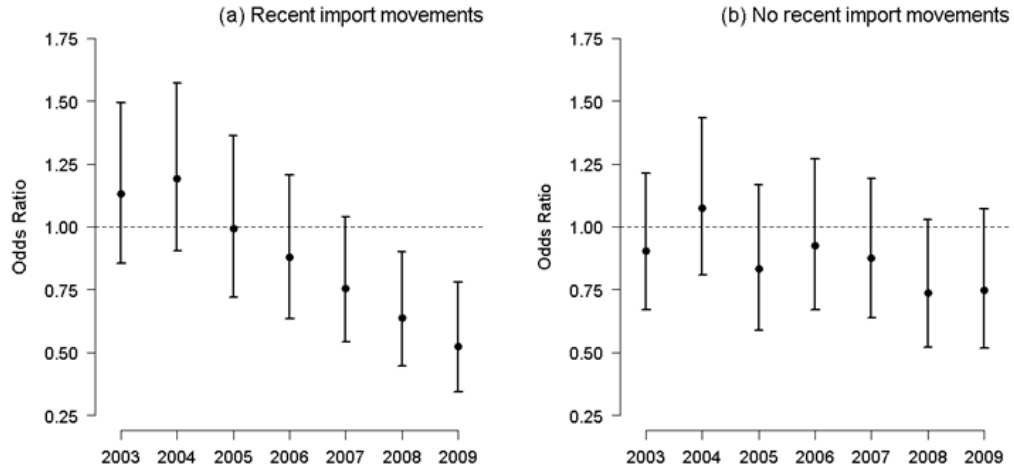
Only 1,727 cattle were identified as positive or inconclusive reactors on SICCT and only 61 cattle were identified as having lesions consistent with bTB at slaughter. Descriptive statistics on the frequency of confirmed breakdowns, unconfirmed breakdowns, and negative RHTs are presented in Figure 3.2. For every RHT with at least one confirmed reactor, there was an average of 21.6 RHTs with unconfirmed reactors (range: 11.5 to 36.0) and 489 RHTs with negative results (range: 190 to 1,064).

Figure 3.2: Frequency of (a) slaughter breakdowns and confirmed RHT breakdowns and (b) unconfirmed RHT breakdowns and negative herds by year.



In tracing the movement history of cattle purchased by farms in the 4 year period prior to testing, 67.4 % of slaughter breakdowns herds, 65.6 % of confirmed RHT herds, 50.9 % of unconfirmed RHT herds, and 34.6 % of negative herds had at least one animal that was imported from overseas or from high incidence parishes of England and Wales. There was a significant downward trend over the study time period in the odds of farms with recent import movements having at least one positive animal identified through RHT or slaughter inspection (Figure 3.3). Using 2002 as the baseline year, farms with recent import movements that were tested in 2009 were 0.52 times less likely to have at least one positive animal compared to herds that were tested in 2002 (95% CI: 0.34 – 0.78, p = 0.002). The risk for herds without recent import movements remained the same from 2002 to 2009.

Figure 3.3: Change in risk of farms (a) with and (b) without recent imports having at least one positive animal.



The average age of cattle identified as reactors on RHT was 6.60 years (median: 5.94, range: 0.81 to 19.68) and 95.3 % were female cattle, whereas the average age of lesioned cattle identified through slaughter inspection was 7.96 years (median: 7.81, range: 1.45 to 17.5) and 85.2% were female cattle. The majority of cattle identified through either surveillance branch were either born in Scotland or located exclusively in Scotland for at least 4 years prior to the test date (Table 3.2). Amongst breakdown herds with complete movement available for all positive animals, 47 of the 58 (81.0%) confirmed RHT breakdowns and 31 out of 45 (72.1%) slaughter breakdowns were identified through cattle that most likely acquired bTB in Scotland.

Table 3.2: Import movement history of individual cattle identified as positive reactors or lesioned at slaughter.

	Slaughter		**Confirmed RHT**		**Unconfirmed RHT**	
Animal origin	N	%	N	%	N	%
Scotland only	36	59.0	94	79.7	1347	83.7
Low incidence parish	1	1.64	0	0.00	2	0.12
High incidence parish	13	21.3	10	8.47	91	5.66
Overseas import	5	8.20	8	6.78	81	5.03
Missing data	7	11.5	6	5.08	88	5.47
Total	**61**	**100**	**118**	**100**	**1609**	**100**

Past movement history was significantly associated with the risk of an individual animal being identified as a reactor on RHT or having lesions at slaughter. Using data from 2006 to 2009, cattle that were located on at least one other farm prior to RHT had 2.18 times greater odds (95% CI: 1.83 – 2.61, $p < 0.001$) of being cases than homebred cattle. Amongst the subset of purchased cattle, those originating from confirmed RHT herds with recent import movements, unconfirmed RHT herds with recent import movements, and unconfirmed RHT herds with no recent import movements were at significantly increased risk of being reactors (Table 3.3). Over 70% of Scottish cattle that reacted to SICCT were located on a Scottish farm at the same time as at least one animal imported from overseas or from high incidence parishes of England and Wales.

Table 3.3: Multivariate logistic regression analyses of animal-level risks associated with movement history amongst purchased cattle.

Movements from:		Cases	Controls	OR	95% CI	p-value
Overseas	No	364	34756	Ref	-	-
	Yes	12	1420	0.85	0.43 – 1.67	0.635
High incidence parish	No	336	32576	Ref	-	-
	Yes	40	3600	1.26	0.87 – 1.83	0.214
Confirmed with imports	No	367	35807	Ref	-	-
	Yes	9	369	2.99	1.31 – 6.76	0.009
Confirmed with no imports	No	375	36016	Ref	-	-
	Yes	1	160	0.85	0.10 – 6.97	0.876
Unconfirmed with imports	No	330	33425	Ref	-	-
	Yes	46	2751	1.63	1.14 – 2.33	0.008
Unconfirmed with no imports	No	359	35246	Ref	-	-
	Yes	17	930	1.85	1.07 – 3.21	0.028
Negative with imports	No	228	19994	Ref	-	-
	Yes	148	16182	0.86	0.68 – 1.09	0.225
Negative with no imports	No	301	28517	Ref	-	-
	Yes	75	7659	0.85	0.64 – 1.13	0.265
Total		**376**	**36176**			

There were a total of 24,094 RHT and slaughter inspection records in the period from 2002 to 2009. Approximately 70 % of all confirmed herds had at least one animal imported from overseas or from high incidence parishes of England and

Wales present on the test date (Table 3.4). In contrast, only 53.4 % of unconfirmed herds and 35.2 % of negative herds had imported cattle, although the percentages were considerably higher when the movement history was traced as far back as possible in the CTS database.

Table 3.4: Presence of imported cattle in confirmed slaughter, confirmed RHT, unconfirmed RHT, and negative RHT observations.

	Slaughter		**Confirmed RHT**		**Unconfirmed RHT**		**Negative RHT**	
Presence of imported cattle:	N	%	N	%	N	%	N	%
On test date	33	71.7	44	72.1	594	53.4	8101	35.2
Four years prior	66	78.2	50	81.9	757	68.1	11483	49.9
All years prior	40	87.0	50	81.9	810	72.9	12655	55.0
Total	**46**	**100**	**61**	**100**	**1111**	**100**	**22983**	**100**

Based on data from 2006 to 2009, farms that purchased at least one animal in the 4 years prior to testing had 2.29 times greater odds (95% CI: 1.41 – 4.02, p = 0.002) of having at least one reactor on RHT or lesioned animal than closed herds. For every $\log_{10}$ increase in the total number of cattle purchased, the odds of having at least one positive animal increased by a factor of 1.65 (95% CI: 1.45 – 1.88, p < 0.001). Open farms that purchased cattle from unconfirmed RHT herds with recent import movements, negative RHT herds with recent import movements, or overseas herds were also at significantly increased risk (Table 3.5). Purchasing cattle from confirmed RHT herds with no recent imports was protective against having at least one reactor identified on RHT (OR: 0.47, 95% CI: 0.27 – 0.79, p = 0.006).

Table 3.5: Multivariate logistic regression analyses of herd-level risks associated with the origin of cattle purchased by open herds.

Movements from:		Cases	Controls	OR	95 % CI	p-value
Overseas	No	299	7654	Ref	-	-
	Yes	97	1434	1.29	1.01 – 1.66	0.045
High incidence parish	No	247	6618	Ref	-	-
	Yes	149	2470	1.16	0.90 – 1.47	0.245
Confirmed with imports	No	324	7862	Ref	-	-
	Yes	72	1226	0.91	0.67 – 1.23	0.556
Confirmed with no imports	No	380	8643	Ref	-	-
	Yes	16	445	0.47	0.27 – 0.79	0.006
Unconfirmed with imports	No	136	4527	Ref	-	-
	Yes	260	4561	1.43	1.12 – 1.84	0.006
Unconfirmed with no imports	No	234	6216	Ref	-	-
	Yes	162	2872	1.11	0.85 – 1.37	0.514
Negative with imports	No	19	1067	Ref	-	-
	Yes	377	8021	1.77	1.11 – 2.97	0.022
Negative with no imports	No	67	1747	Ref	-	-
	Yes	329	7341	0.84	0.63 – 1.13	0.232
Total		**396**	**9088**			

The univariate case-case comparisons revealed significant differences in the demographic profile of confirmed RHT herds and unconfirmed RHT herds (Table 3.6). In general, confirmed RHT herds had a greater number of cattle present, a greater number of cattle tested, and a greater proportion of animals in the herd that were imported from high incidence regions. Being located in northern and eastern parts of Scotland was associated with decreased odds of being a confirmed RHT herds. In the multivariate analysis (Table 3.8a), for every 1% increase in the percentage of imported cattle in the herd, the odds of being confirmed increased by a factor of 1.02 (95% CI: 1.01 – 1.03, $p < 0.001$) and for every 100 km moved east in Scotland, the odds of being confirmed decreased by a factor of 0.59 (95% CI: 0.40 – 0.88, $p < 0.001$).

Table 3.6: Univariate case-case comparison between confirmed and unconfirmed RHT herds.

Variable	Confirmed	Unconfirmed	OR	95% CI	p-value
Number of cattle tested	59	904	2.07	1.12 – 3.89	0.022
Number of cattle present	59	904	2.35	1.27 – 4.46	<0.001
% imported cattle	59	904	1.02	1.01 – 1.03	0.002
Number of cattle moved on	59	904	1.23	0.85 – 1.79	0.274
Farms within 5 km radius	59	904	0.91	0.46 – 1.96	0.795
Test status of neighbours					
Negative herds	11	177	Ref	-	-
Unconfirmed herds	34	501	1.09	0.56 – 2.30	0.806
Confirmed herds	14	226	0.99	0.44 – 2.30	0.994
Northing coordinate	59	904	0.72	0.56 – 0.93	0.013
Easting coordinate	59	904	0.69	0.48 – 1.00	0.050
Herd type					
Beef	20	387	Ref	-	-
Beef fattening	0	7	NA	-	-
Beef suckler	24	351	1.32	0.72 – 2.46	0.369
Dairy	15	156	1.86	0.91 – 3.71	0.080
Mixed	0	3	NA	-	-
Average number of sheep	59	904	0.95	0.79 – 1.15	0.605
Average number of poultry	59	904	0.73	0.32 – 1.36	0.409

The univariate case-control comparisons revealed several demographic factors associated with an increased odds of having unconfirmed reactors disclosed on RHT (Table 3.7), the majority of which were also significant in the multivariate model (Table 3.8b). Compared to negative RHT herds, unconfirmed RHT herds had a greater percentage of imported cattle in the herd and a greater number of cattle tested. The presence of at least one other herd with confirmed or unconfirmed results within a 5 km radius increased the odds of having an unconfirmed RHT by approximately 1.85. However, the odds decreased with the total number of other farms present in a 5 km radius (OR: 0.45, 95% CI: 0.36 – 0.57, $p < 0.001$). Similar to the case-case comparison, herds located in the eastern parts of Scotland were at decreased odds of having unconfirmed reactors (OR: 0.85, 95% CI: 0.76 – 0.95, $p <$

0.001). Higher average numbers of poultry on the farm were also associated with decreased odds of being an unconfirmed herd.

Table 3.7: Univariate case-control comparison between unconfirmed and negative RHT herds.

Variable	Unconfirmed	Controls	OR	95% CI	p-value
Number of cattle tested	904	9969	4.54	3.92 – 5.28	< 0.001
Number of cattle present	904	9969	3.39	2.92 – 3.83	< 0.001
% imported cattle	904	9969	1.02	1.01 – 1.03	< 0.001
Number of cattle moved on	904	9969	1.73	1.58 – 1.89	< 0.001
Farms within 5 km radius	904	9969	0.82	0.69 – 0.98	0.031
Test status of neighbours					
Negative herds	177	3203	Ref	-	-
Unconfirmed herds	501	4954	1.83	1.54 – 2.19	< 0.001
Confirmed herds	226	1812	2.26	1.84 – 2.77	< 0.001
Northing coordinate	904	9969	0.77	0.73 – 0.81	< 0.001
Easting coordinate	904	9969	1.07	0.98 – 1.16	0.132
Herd type					
Beef	387	4425	Ref	-	-
Beef fattening	7	179	0.45	0.19 – 0.89	0.038
Beef suckler	351	4082	0.98	0.85 – 1.14	0.825
Dairy	156	1276	1.40	1.15 – 1.70	< 0.001
Mixed	3	7	4.90	1.05 – 17.7	0.022
Average number of sheep	904	9969	1.21	1.15 – 1.28	< 0.001
Average number of poultry	904	9969	0.69	0.58 – 0.80	< 0.001

Overall, there was a strong positive correlation between the total number of cattle present on the farm on the studied test date and the number of individual RHTs performed between 2002 and 2009 ($r = 0.88$, $p < 0.001$). However, there was only moderate correlation between the total number of cattle present and the total number of cattle moved onto the farm in the last 4 years ($r = 0.72$, $p < 0.001$).

Table 3.8: Multivariate (a) case-case comparison between confirmed unconfirmed RHT herds and the (b) case-control comparison between unconfirmed and negative RHT herds.

Variable	OR	95% CI	p-value
(a) Case-case comparison			
% imported cattle	1.02	1.01 – 1.03	< 0.001
Easting coordinate	0.59	0.40 – 0.88	< 0.001
(b) Case-control comparison			
% imported cattle	1.01	1.00 – 1.02	< 0.001
Number of cattle tested	4.34	3.65 – 5.19	< 0.001
Farms within 5 km radius	0.45	0.36 – 0.57	< 0.001
Test status of neighbours			
Negative herds	Ref	-	-
Unconfirmed herds	1.85	1.52 – 2.27	< 0.001
Confirmed herds	1.85	1.46 – 2.34	< 0.001
Easting coordinate	0.85	0.76 – 0.95	0.003
Herd type			
Beef	Ref	-	-
Beef fattening	0.70	0.29 – 1.43	0.376
Beef suckler	0.95	0.81 – 1.12	0.568
Dairy	0.71	0.57 – 0.89	0.002
Mixed	1.74	0.36 – 6.56	0.436
Average number of poultry	0.85	0.73 – 0.99	0.042

Discussion

The main objective of this analysis was to investigate the effects of routine surveillance design on the potential for imported bTB to spread within and between cattle herds in a low incidence region. Scotland provided an interesting case study because of the significant demographic and legislative changes that occurred in the years leading up to OTF recognition in 2009. When the movement restrictions for foot-and-mouth disease were lifted in November 2001, there was an influx of cattle from endemic tuberculosis regions in other parts of Great Britain to replace animals that were culled as part of disease eradication measures. In other regions of Great Britain, re-stocking has been linked to an increased incidence of new bTB

breakdowns (Carrique-Mas et al., 2008) and it is likely that many of these imported cattle were responsible for introducing bTB into Scotland. This is supported by the greater number of confirmed bTB breakdowns identified through RHT and slaughter surveillance from 2002 to 2005.

Given the strong association between cattle import movements and confirmed breakdowns in low incidence regions (Gopal et al., 2006; Green et al., 2008; Schiller et al., 2011), legislation was introduced in September 2005 that required all cattle imported from high incidence parishes of England and Wales to be tested for bTB within 120 days of arriving in Scotland. Previous work has shown that the financial and logistical constraints associated with post-movement testing have significantly reduced the number of cattle imported into Scotland each year (Bennett, 2009; Gates et al., 2013). In the period from 2006 to 2009, herds that purchased cattle from high incidence parishes in the 4 years prior to testing were found to be at no greater risk of having reactors disclosed on RHT than herds with no recent import movements. However, herds that imported cattle from overseas were still at significantly increased risk despite the fact that post-movement testing for this category was required throughout the study time period. This highlights potential issues with the sensitivity of SICCT for detecting infected cattle and the importance of the complementary pre-movement testing legislation that was introduced to England and Wales in May 2006 (de la Rua-Domenech et al., 2006; Clegg et al., 2008).

The risk of herds with recent import movements having unconfirmed reactors disclosed on RHT also decreased following the introduction of pre- and post-movement testing legislation, which suggests that an unknown, but potentially significant number of unconfirmed cases were truly infected with bTB. Over 50 % of unconfirmed herds had at least one imported animal present on the RHT test date and in tracing the complete movement history of animals present in the herd prior to the RHT date, an additional 22 % of unconfirmed RHTs could be linked to past cattle import movements. One of the many limitations in conducting RHTs at 4-

year intervals is that infected cattle may be introduced to the herd and subsequently slaughtered or sold prior to the next RHT. At most, only 23% of cattle present in Scotland from 2002 to 2009 were subject to SICCT. The actual figure may be substantially lower since individual cattle may be tested multiple times in different herds over their lifespan (Mitchell, 2006) (this was not possible to detail in the current study because the results of negative RHTs were recorded *en masse*). It is also worth noting that cattle over 30 months of age account for fewer than 17% of all cattle slaughtered at abattoirs, but over 64% of those identified with visible lesions.

Based on data from the confirmed RHT and slaughter case herds, there was evidence that on-farm transmission takes place in the delay between disease introduction and detection in Scotland. Approximately 75% of confirmed breakdowns were identified through cattle with no import movement history. Similar findings have been reported in other low incidence regions (Gopal et al., 2006). For examples, Fischer and colleagues document an outbreak in the Netherlands where the import of an infected animal generated a single additional case detected 392 days later (Fischer et al., 2005). The introduction of a single infected animal to a New Zealand dairy herd resulted in eight further confirmed reactors identified over a two year period (Barlow et al., 1997). With the high frequency of movements between Scottish cattle farms (Volkova et al., 2010), there is a risk that exposed cattle will be sold to other herds prior to detection and generate secondary outbreaks in the receiving herd.

Other case-control studies from endemic regions have shown that cattle purchased from herds with previously disclosed reactors were significantly more likely to react positively on subsequent herd tests (Ramírez-Villaescusa et al., 2008; Wolfe et al., 2009). In the current analysis, it was shown that individual cattle purchased from herds with confirmed and unconfirmed RHT results were at increased risk of being identified as unconfirmed reactors on RHT compared to other cattle located on at least one other farm prior to testing. Age and gender were

included in the logistic regression models to account for biases introduced by the criteria for selecting animals to test on RHT. Older female cattle are at increased risk of being reactors as well as being tested (Green et al., 2012). On the other hand, at the herd-level, the presence of imported cattle in the Scottish source herds was a risk factor for unconfirmed breakdowns regardless of the source herd's RHT status. If the animals were only recently infected, the sensitivity of tuberculin testing, slaughter inspections, and tissue cultures would be expectedly low (Byrne, 1992). Outbreaks in herds also tend to be less severe when the infected animal is purchased rather than bred in the herd (Olea-Popelka et al., 2008), which means there may be fewer other infected cattle to confirm the presence of bTB.

Herds that disclose unconfirmed reactors or inconclusive reactors on RHT represent a unique regulatory challenge in low incidence regions. In this analysis, there were more than 20 unconfirmed RHT breakdowns for every confirmed RHT breakdown. The costs associated with cattle movement restrictions, contact tracing, and short interval tests can be significant for both the farmer and the taxpayer (Bennett and Cooke, 2005), especially since unconfirmed breakdowns tend to occur in larger herds with a central role in the cattle trade network (Dommergues et al., 2012). As expected, the total number of cattle subject to RHT was one of the strongest risk factors for identifying unconfirmed reactors, but also highly correlated with the total number of cattle present in the herd from 2002 to 2009 and moderately correlated with the total number of cattle moved onto the farm. It is therefore difficult to determine whether large herds are at risk simply because of surveillance design (Monaghan et al., 1994) or whether there are other management factors that predispose large herds to having more frequent or more severe bTB breakdowns (White and Benhin, 2004; Brooks-Pollock and Keeling, 2009; Wolfe et al., 2010).

The case-control comparisons revealed several interesting spatial trends in the epidemiology of bTB in Scotland. Herds in the eastern and northern parts of Scotland were significantly more likely to have confirmed but less likely to have unconfirmed reactors, which may be related to the spatial distribution of cattle

imported from Ireland or Northern Ireland and cattle imported from high incidence parishes of England and Wales, respectively. In areas with greater exposure to high risk cattle, there may be greater potential for silent spread through unregistered movements between neighbouring herds and other local transmission mechanisms (Brennan et al., 2008).

With farms georeferenced as a point location, it was not possible to assess potential for fence-line contacts and hence the aggregate variable of bTB status of all farms within a 5km radius was considered. Similar to studies in other low incidence regions, there was evidence of spatial effects in bTB surveillance results (Munroe et al., 1999; Perez et al., 2002; Green and Cornell, 2005). Herds with at least one neighbour that disclosed unconfirmed reactors through RHT were significantly more likely to have unconfirmed reactors themselves. There are several possible explanations for these findings. First, neighbouring herds may be more likely to purchase cattle from similar sources or trade directly with each other. Second, there may be other cross-reacting mycobacterial antigens in the production environment, such as *M. avium* subsp. *paratuberculosis* (Aranez et al., 2006) *or M. caprae* (Muñoz Mendoza et al., 2012), that can lead to false positive reactions. Third, test interpretation is often subjective and veterinarians may be more likely to classify an animal as a positive or inconclusive reactor if there is a history of bTB in neighbouring herds (Humblet et al., 2011). Finally, the presence of wildlife reservoirs for bTB within the local farm environment cannot be ruled out although none have yet been identified in Scotland.

There were several challenges in using CTS movement data to determine the most likely origin of confirmed and unconfirmed bTB breakdowns. Surveillance results are stored in the VETNET database under the main farm CPH number regardless of whether cattle are housed on that location or on other uniquely identified land parcels operated by the same cattle business (Madders, 2006). Several of the study farms were excluded from the analysis because the CPH code could not be linked to a valid CTS location identifier or no cattle were present on the

location at the time of testing. Furthermore, farmers that have registered for 'linked holding' status are not required to report the movements of cattle between land parcels, which may have underestimated potential exposures to imported cattle or cattle moved from other breakdown herds. Similar issues were encountered in linking the movement data with the agricultural census data, which highlights the need to develop a more unified approach for recording national animal health data so it can be used more effectively in future epidemiological research.

Conclusion

Limitations in the sensitivity and specificity of routine surveillance methods for bTB have been highlighted as one of the major barriers to eradicating disease from low incidence regions (Gordejo and Verneersch, 2006; Schiller et al., 2011). In this analysis, there was evidence that bTB spreads within and between Scottish cattle herds at low levels due to the delay in detecting infected cattle through routine tuberculin herd testing or slaughter inspection. However, as several analyses have shown, the costs of increasing surveillance intensity often greatly exceed the potential costs incurred from silent spread (Fischer et al., 2005; van Asseldonk et al., 2005; Clegg et al., 2008; Welby et al., 2012). Herds with unconfirmed reactors represent a particular control challenge as many of the risk factors associated with confirmed bTB breakdowns, including herd size and cattle movements, also increase the likelihood of detecting false positive reactors. Targeted surveillance of cattle imported from high incidence regions appears to be an effective strategy for reducing risk, but requires both pre- and post-movement testing to increase test sensitivity. The evidence of spatial clustering of herds with unconfirmed reactors warrants further investigation into environmental or management factors that may interfere with test interpretation as bTB is not currently known to be present in Scottish wildlife reservoirs.

Chapter 4

Associations of movements, local spread, and biosecurity with bovine viral diarrhoea virus seropositivity[1]

Summary

The success of bovine viral diarrhoea virus (BVDV) eradication campaigns can be undermined by spread through local transmission pathways and poor farmer compliance with biosecurity recommendations. This work combines recent survey data with cattle movement data to explore the issues likely to impact on the success of BVDV control in Scotland. In this analysis, data from 249 beef suckler herds and 189 dairy herds in Scotland were studied retrospectively to determine the relative association of cattle movements, local spread, and biosecurity with BVDV seropositivity. Multivariate logistic regression models revealed that cattle movement risk factors explained approximately 3 times more residual deviance than risk factors for local spread amongst beef suckler herds, but only 0.78 times as much residual deviance as risk factors for local spread amongst dairy herds. These findings are most likely related to differences in cattle husbandry practices and suggest that where financial prioritization is required, focusing on reducing movement-based risk is likely to be of greatest benefit when applied to beef suckler herds. The reported use of biosecurity measures such as purchasing cattle from BVDV accredited herds only, performing diagnostic screening at the time of sale, implementing isolation periods for purchased cattle, and installing double fencing on shared field boundaries had minimal impact on the risk of herds being seropositive for BVDV. Only 28% of beef farmers and 24% of dairy farmers with seropositive

[1] This chapter is a modified version of the following publication: Gates, M.C., Woolhouse, M.E.J., Humphry, R.W., Gunn, G.J. 2013. Relative associations of cattle movements, local spread, and biosecurity with bovine viral diarrhoea virus (BVDV) seropositivity in beef and dairy herds. Preventive Veterinary Medicine (In press).

herds recognized that their cattle were affected by BVDV and those that did perceive a problem were no less likely to sell animals as replacement breeding stock and no more likely to implement biosecurity measures against local spread than farmers with no perceived problems. In relation to the current legislative framework for BVDV control in Scotland, these findings emphasize the importance of requiring infected herds take appropriate biosecurity measures to prevent further disease transmission and conducting adequate follow-up to ensure that biosecurity measures are being implemented correctly in the field.

Introduction

Scotland launched the first phases of a bovine viral diarrhoea virus (BVDV) eradication campaign in September 2010 as part of an industry led effort to reduce the impact of disease on herd health and productivity. Under current guidelines, all cattle breeding herds must be screened for BVDV by February 2013 and annually thereafter to monitor changes in herd infection status (Anonymous, 2013). Farmers that subsequently choose to sell cattle in Scotland will be required to declare the BVDV status of their herd at the time of sale to provide buyers with the option of sourcing replacement cattle exclusively from low risk herds or implementing additional biosecurity measures to prevent disease transmission through cattle purchased from high risk herds. This legislation is based on empirical evidence that sourcing heifers or pregnant dams from herds with an unknown BVDV status significantly increases the risk of disease outbreaks (Valle et al., 1999; Fray et al., 2000; Luzzago et al., 2008). Depending on the initial industry response, additional control measures may be introduced, such as requiring farmers with BVDV positive herds to test individual cattle for persistent infections (PI) prior to movement or to limit contact with neighbouring cattle by installing double fencing on shared field boundaries.

The experiences of other countries and regions undergoing BVDV eradication have shown that control can rarely be achieved in the absence of such compulsory legislation (Bitsch et al., 2000; Hult and Lindberg, 2005; Lindberg et al., 2006; Truyers et al., 2010). Farmers with BVDV positive herds may be reluctant to implement control measures if the herd is not experiencing significant reproductive losses, if there is no change in the market value of cattle sold from accredited BVDV free herds, and if there is a risk of disease being reintroduced from neighbouring herds with PI cattle (Smith and Grotelueschen, 2004; Heffernan et al., 2008). Farmers with BVDV negative herds may also be reluctant to implement preventive measures if the perceived risk of introducing disease is low and if the biosecurity measures are thought to be too costly or ineffective (Santarossa et al., 2005; Negrón et al., 2011). Irrespective of the herd's serological status, there is still an increased risk of disease transmission if the biosecurity measures are not implemented according to recommended guidelines.

Assessing the relative contribution of different transmission mechanisms to BVDV spread and the relative efficacy of the corresponding biosecurity measures under field settings can provide policymakers with valuable information on how to allocate limited disease control resources more effectively over the course of an eradication programme. This is particularly important since any transmission through fence-line contact, airborne spread, shared equipment, and other undocumented sources can undermine the efficacy of programmes based on pre-movement testing and movement restrictions alone (Bitsch et al., 2000; Ståhl et al., 2005). In this analysis, data from 249 Scottish beef suckler herds and 189 Scottish dairy herds that participated in national seroprevalence studies from October 2006 through May 2008 were analyzed retrospectively (1) to determine the relative importance of cattle movements and local spread to herd serological status and (2) to characterize the use and efficacy of biosecurity measures against transmission through cattle movements or local spread.

Methods

Study herds

Two national studies were conducted between October 2006 and May 2008 to estimate the seroprevalence of BVDV amongst herds in the Scottish beef suckler and dairy industries (Brulisauer et al., 2010; Humphry et al., 2012). A total of 301 herds participated in the beef suckler study and 374 herds participated in the dairy study. During the farm visit for beef suckler herds, blood samples were taken from approximately 10 randomly selected cattle between 6 and 16 months of age and processed using an indirect BVDV antibody ELISA to obtain antibody titres on each individual. Based on statistical criteria previously described for these data (Brulisauer et al., 2010), the 225 herds with no serological evidence of active infection in young stock were considered control herds and the remaining 76 herds with a within-group prevalence of more than 26.3% were considered seropositive case herds.

For dairy herds, bulk milk tank samples were obtained directly through the farm's milk purchaser at the time of collection and processed using an indirect BVDV antibody ELISA to obtain the percentage positivity (PP) scores. Based on the Swedish BVDV eradication class system, the 220 unvaccinated herds were assigned into one of four groups based on their PP score. The scores ranged from Class 0 herds, considered unlikely to include any seropositive animals and indicating a low probability of BVDV infection, to Class 3 herds, considered highly likely to have many seropositive animals indicating a recent or active infection. For the purpose of this analysis, the 77 herds designated as Class 0 or Class 1 were considered control herds and the remaining 143 herds designated as Class 2 or Class 3 were considered seropositive case herds.

Study variables

All farmers were required to complete a basic questionnaire to assess whether specific management practices contributed to the risk of being seropositive

for BVDV. Copies of the original beef suckler questionnaire and dairy questionnaire are provided in Appendix A and B, respectively. This analysis focuses on the subset of questions related to local spread, biosecurity, and BVDV history including whether the farmer thought their herd was affected by BVDV. These survey questions all required simple binary 'yes' or 'no' responses.

The local spread variables included the presence of public footpaths crossing the farm, cattle drinking water from ponds or watercourses shared with other farms, the use of relief stockman that come in contact with livestock from other farms, sharing pasture with other farms, sharing equipment with other farms, the observation of deer grazing in close proximity, and the presence of a sheep enterprise on the farm.

The biosecurity variables were divided into two categories; those designed to reduce transmission through cattle movements and those designed to reduce transmission through local spread. For movement biosecurity, these included purchasing cattle exclusively from BVDV accredited herds, performing blood or other diagnostic screening at purchase, and implementing an isolation period for all purchased stock. For biosecurity against local spread, these included double fencing shared field boundaries to prevent nose-to-nose contact with neighbouring herds, restricting access of non-essential visitors, enforcing strict disinfection measures for essential visitors, and providing separate pick-up and drop-off areas for delivery vehicles.

Records from the Cattle Tracing System (CTS) database were used to generate estimates of the total number of replacement cattle moved onto the farm by production type (open heifer, pregnant heifer, open cow, pregnant cow, breeding bull, or store cattle) and the average farm size during the three year period prior to sampling. This time window was chosen based on published estimates of the average time from disease introduction to clearance (Ezanno et al., 2008; Tinsley et al., 2012). A heifer was defined as a female animal with no prior calvings that either subsequently delivered a calf or survived beyond 30 months of age. A cow was

defined as a female with at least one prior calving. Heifers and cows that were less than 280 days from the next recorded calving date at the time of movement were considered pregnant. Breeding bulls included male animals that survived beyond 30 months of age, while store cattle included any male or female animals with no recorded calvings that were slaughtered before 30 months of age. It was assumed that animals slaughtered before 30 months of age were intended for beef production based on food safety legislation in Great Britain during the study time period that prevented animals over 30 months of age from entering the human food chain. The movement variables were subsequently converted into binary categorical variables. Information on whether cattle attended shows, whether the farm grazed cattle away from the main holding, and whether the farm sold cattle as replacement breeding stock was also available from the questionnaire responses for both herd types.

To link the serological results with the corresponding cattle movement data, the main farm address reported in the management questionnaire had to be matched against a database of county-parish-holding (CPH) codes provided by the Scottish government. A list of all farm locations in Scotland that housed cattle from October 2006 through May 2008 was also extracted from the CTS database. The CPH codes were used to obtain spatial easting and northing coordinates from one of three available databases: the Postal Address File database, the Scottish land fields database, or the VETNET database. This information was used to generate estimates of the total number of farm locations with breeding cattle and the total number of farm locations with store cattle within a 10km radius of each study herd. It should be noted that a single farm business may house cattle on multiple locations with unique CPH codes and some CPH codes are only used to house cattle temporarily, which may overestimate the density of cattle herds. Farms for which there was no available CPH code, an obvious discrepancy between the survey estimates of herd size and CTS database estimates of herd size, or no available farm coordinate data were excluded leaving 249 beef suckler herds (65 case herds and

184 control herds) and 185 dairy herds (119 case herds and 66 control herds) in the final sample.

Statistical analyses

Data from the beef suckler herds and dairy herds were analyzed separately throughout the study due to underlying differences in the sampling methodology, the definition of a seropositive herd, and other sector related management practices that are known to be associated with BVDV seropositivity. General descriptive statistics are provided for all study variables including the mean, median, and range for the continuous variables and the percentage of positive responses for all categorical variables. The variables 'total number of cattle purchased', 'total number of breeding farms within a 10 km radius', and 'total number of other farms within a 10 km radius' were log transformed prior to analysis due to the highly right skewed distributions. The associations between pairs of study variables were assessed using Pearson's product moment correlations for continuous-continuous pairs, one-way analysis of variance for continuous-categorical pairs, and χ^2 analysis for categorical-categorical pairs. Associations with a p-value < 0.05 were considered statistically significant.

To assess the relative importance of different transmission mechanisms to seropositivity, three multivariate logistic regression models were created: one that contained all the risk factor variables associated with cattle movements, one that contained all the risk factor variables associated with local spread, and one that combined all movement and local spread risk factors. The percentage change in deviance, calculated as the difference between the null deviance and the residual deviance divided by the null deviance, was recorded for each model and used as an indication of the explanatory power of each variable set. The explanatory power of each individual risk factor variable was also assessed using the same methodology. The univariate odds ratios and corresponding 95% confidence intervals (CIs) were also reported as a measure of effect size.

Univariate logistic regression analyses were also used to assess the associations between biosecurity measures and the risk of herds being seropositive for BVDV and other associations with biosecurity utilization. Variables that were associated with the outcome of interest at a p-value < 0.05 were considered statistically significant.

Results

Descriptive statistics

There were significant differences in the demographic characteristics of Scottish beef suckler and dairy herds. Beef suckler herds contained an average of 223 cattle (median: 172) and purchased an average of 88 cattle (median: 28) over the three years prior to sampling. In contrast, dairy herds contained an average of 345 cattle (median: 290) and purchased an average of 54 cattle (median: 8) over the same time period. Only 9 of the 249 beef suckler herds (4%) and 29 of the 185 dairy herds (16%) remained completely closed to replacement cattle purchases. The frequency distributions of herd sizes and total number of cattle movements are presented in Figure 4.1 .

The spatial distribution of beef and dairy breeding dams in Scotland is shown in Figure 4.2. The dairy industry is highly concentrated in the south west and border regions, while the beef industry is more geographically dispersed. Beef suckler herds had an average of 74 farms (median: 67, range: 3 to 191) with breeding cattle and 18 farms (median: 14, range: 1 to 91) with store cattle only within a 10 km radius of the main farm location. In contrast, dairy herds had an average of 100 farms (median: 94, range: 13 to 197) with breeding cattle and 20 farms (median: 17, range: 1 to 94) with store cattle only within a 10 km radius of the main farm location.

Figure 4.1: Frequency distribution of the (a) average herd size and (b) total number of cattle movements for beef suckler herds and dairy herds.

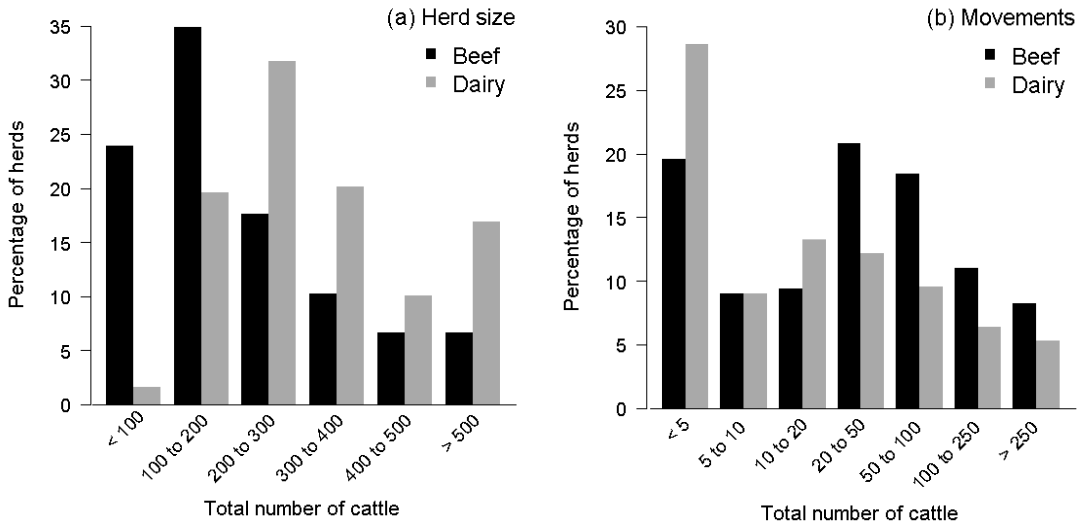
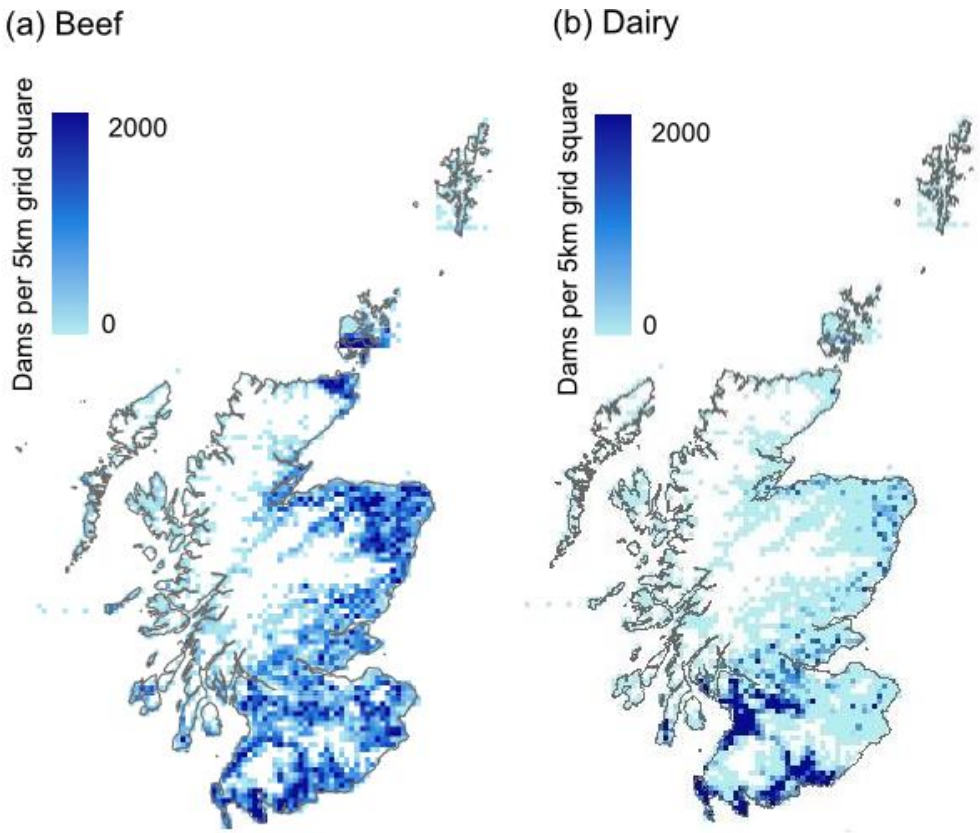


Figure 4.2: Spatial distribution of (a) beef and (b) dairy breeding dams in Scotland during 2007 expressed in units of total number of dams per 5 km grid square.



The prevalence of movement risk factors and risk factors for local spread amongst the study herds are presented in Table 4.1. Overall, 15.4% of replacement breeding females purchased by beef suckler herds were pregnant, while 28.1% of replacement breeding females purchased by dairy herds were pregnant. Over 40% of all beef suckler and dairy herds reported grazing cattle away from the main farm holding. The presence of public footpaths, shared ponds, and deer grazing in close proximity were the most commonly reported risk factors for local spread amongst beef suckler and dairy herds. Over 75% of beef suckler herds also maintained a sheep enterprise.

Table 4.1: Prevalence of (a) movement risk factors and (b) risk factors for local spread amongst beef suckler herds and dairy herds.

(a) Movement risk factors	% of herds		(b) Risk factors for local spread	% of herds	
	Beef	Dairy		Beef	Dairy
Open heifers	44.2	34.6	Public footpaths	49.4	42.1
Pregnant heifers	22.9	23.2	Shared ponds	50.2	47.0
Open cows	36.9	32.4	Relief stockman	28.5	34.1
Pregnant cows	22.1	14.6	Shared pasture	16.9	19.5
Store cattle	30.2	23.7	Shared equipment	30.1	22.2
Bulls	83.9	58.9	Deer grazing	72.3	52.4
Attend shows	12.4	14.1	Sheep enterprise	77.1	34.1
Grazed away	44.2	41.6			

In general, farms that purchased one type of cattle were significantly more likely to purchase other types of cattle as well and there were strong associations between the total number of cattle purchased and each of the animal type movement variables. Beef suckler herds that grazed cattle away from the farm had significantly greater odds of sharing pasture with other herds (OR: 3.05, 95% CI: 1.54 – 6.29, $p = 0.001$). Beef suckler and dairy herds that reported sharing equipment also had greater odds of sharing pasture (OR: 2.27, 95% CI: 1.12 – 4.40, $p = 0.021$ and OR: 3.98, 95% CI: 1.80 – 8.74, $p < 0.001$, respectively). For beef suckler herds, there was a weak positive correlation between the total number of cattle moved onto the farm and both the total number of breeding farms within a 10 km radius ($r = 0.176$, p

= 0.005) and the total number of other farms within a 10 km radius (r = 0.179, p = 0.005). The opposite effect was seen for dairy herds. There was a weak negative relationship between the total number of cattle moved onto the farm and total number of breeding farms within a 10km radius (r = -0.165, p = 0.022).

Only 28% of beef suckler farmers and 24% of dairy farmers with seropositive herds thought their cattle were affected by BVDV (Table 4.2). Of the herds that were thought to be affected by BVDV, 64% of beef suckler herds and 15% dairy herds were actually seronegative at the time of sampling. Of the herds that were thought to be unaffected by BVDV, 23% of beef suckler herds and 57% dairy herds were actually seropositive at the time of sampling.

Table 4.2: Descriptive statistics on the farmer perception of herd BVDV status and the true serological status of (a) beef suckler herds and (b) dairy herds.

(a) Beef suckler		Serological status		(b) Dairy		Serological status	
		+	–			+	–
Farmer perception	Affected	18	32	Farmer perception	Affected	29	5
	Unaffected	34	112		Unaffected	33	25
	Don't know	13	40		Don't know	57	36

Relative importance of movements versus local spread

Results from the univariate analyses of movement and local spread risk factors associated with BVDV seropositivity are shown in Figure 4.3. In general, purchasing cattle of any production type was associated with a significantly increased risk of being seropositive with the exception of open heifers and bulls for beef herds and pregnant heifers for dairy. For every $\log_{10}$ increase in the total number of cattle moved on, the odds being seropositive increased by a factor of 3.21 for beef herds (95% CI: 2.02 – 5.31, p < 0.001) and 1.82 for dairy herds (95% CI: 1.20 – 2.83, p = 0.005). None of the categorical local spread variables were significant at the 0.05 level for beef herds. However, for dairy herds, the presence of public footpaths significantly decreased the risk of being seropositive (OR: 0.45,

95% CI: 0.24 – 0.84, p = 0.012). For every $\log_{10}$ increase in the total number of breeding farms within a 10 km radius, the odds being seropositive increased by a factor of 3.64 for beef herds (95% CI: 1.13 – 13.2, p = 0.038) and 13.5 for dairy herds (95% CI: 3.51 – 57.1, p < 0.001).

For beef suckler herds, the addition of all cattle movement variables into the multivariate logistic regression model reduced the deviance by 11.9%, whereas the addition of all local spread variables reduced the model deviance by only 4.0%. When all movement and local spread variables were combined, the model deviance was reduced by 14.2%. Markedly different trends were observed for dairy herds where the addition of all cattle movement variables reduced the model deviance by 9.7% and the addition of all local spread variables reduced the model deviance by 12.4%. In combination, the movement and local spread variables reduced the model deviance by 23.9%. The changes in model residual deviance following the addition of each variable alone and in combination are presented in Figure 4.4.

Biosecurity for cattle movements

Overall, 80% of the 240 open beef suckler herds and 45% of the 156 open dairy herds implemented at least one biosecurity measure to prevent BVDV transmission through cattle movements. There was weak evidence that beef suckler herds were less likely to implement at least one movement biosecurity measures as the log transformed total number of purchased cattle increased (OR: 0.64, 95% CI: 0.40 – 1.02, p = 0.062). This association was not significant for dairy herds (OR: 0.96, 95% CI: 0.63 – 1.47, p = 0.874). Only 38 of the 181 beef suckler herds (21%) that isolated stock after purchase and 11 of the 62 dairy herds (18%) that isolated stock after purchase also performed diagnostic screening.

Figure 4.3: Odds ratios (•) and 95% confidence intervals (–) from the univariate analyses of risk factors for BVDV seropositivity in (a) beef suckler herds and (b) dairy herds. Note that the upper confidence interval for the total number of breeding farms within 10 km of a dairy herd (*) has been truncated from 57.1.

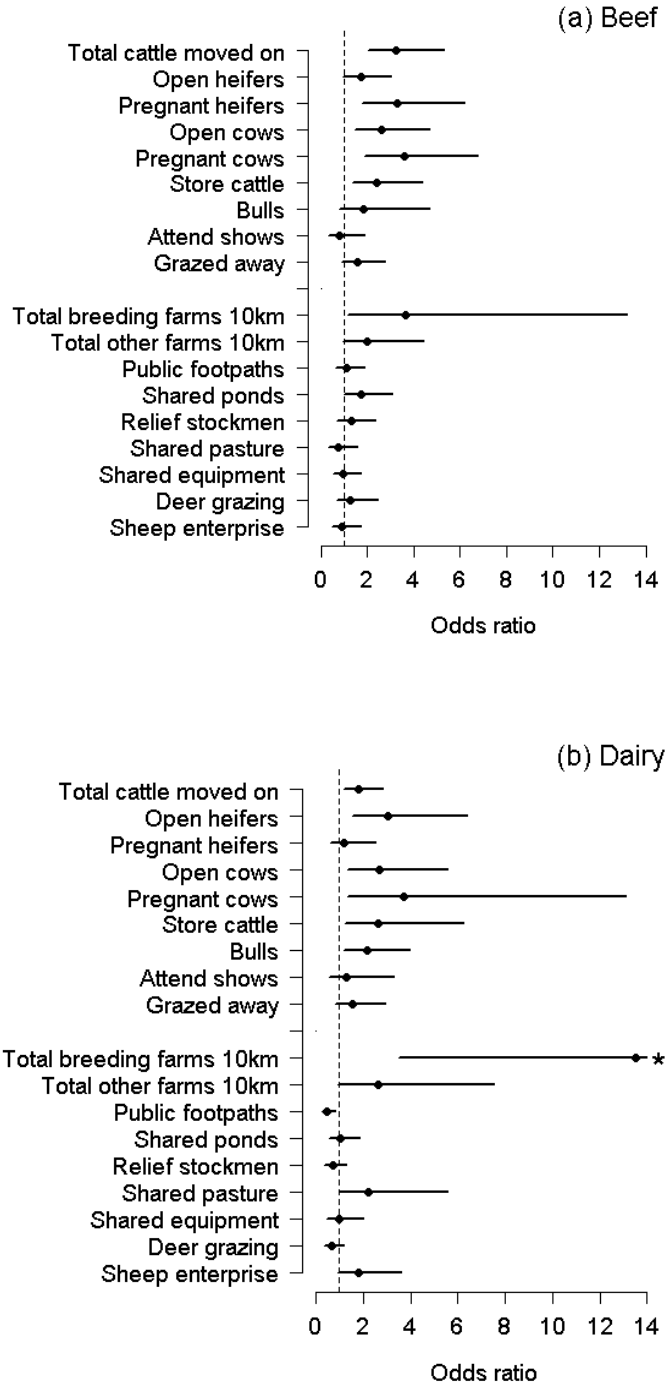
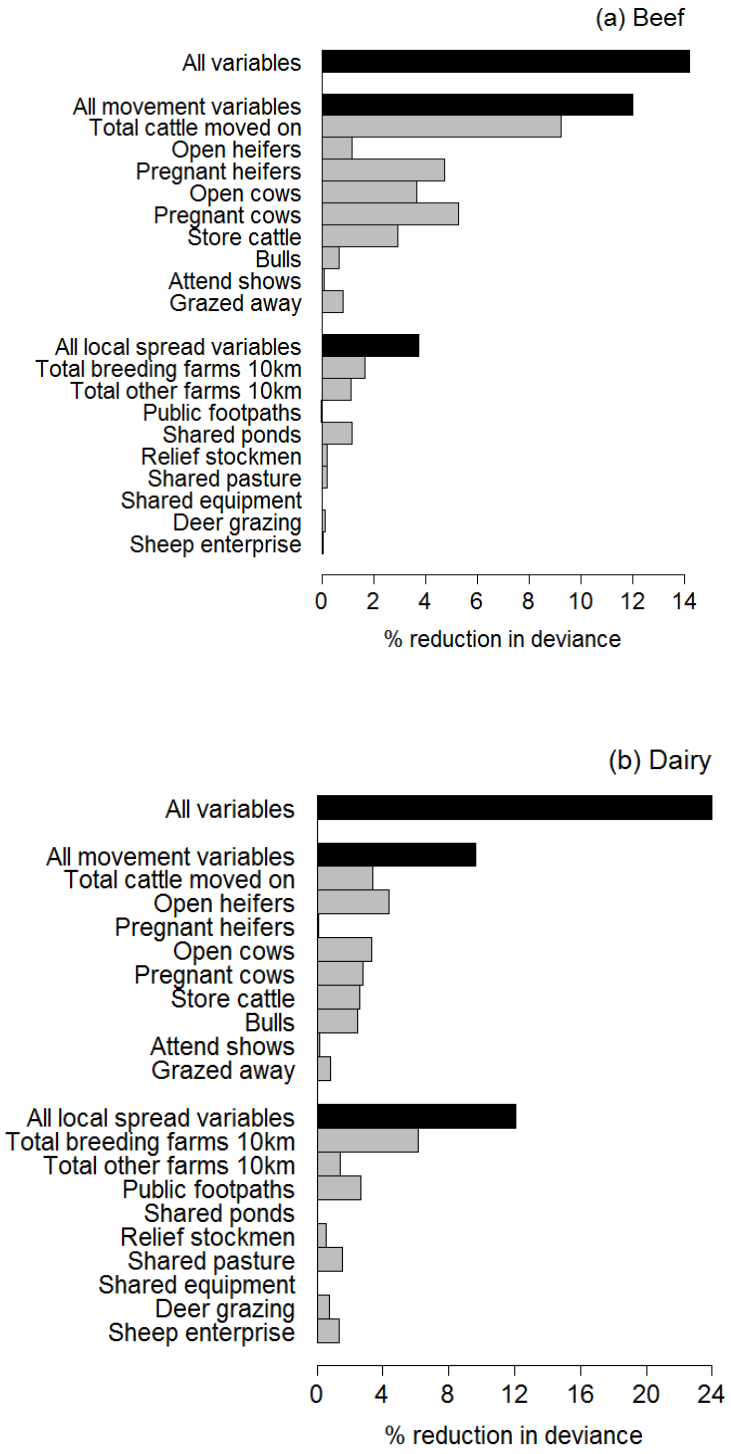


Figure 4.4: Change in model residual deviance following the addition of movement and local spread variables alone (grey) or in combination (black) for (a) beef suckler herds and (b) dairy herds.



In the univariate analysis for beef suckler herds, none of the biosecurity measures significantly decreased the risk of being seropositive for BVDV (Table 4.3). Dairy herds that performed diagnostic screening of purchased cattle were significantly less likely to be seropositive for BVDV (OR: 0.21, 95% CI: 0.05 – 0.69, p = 0.013). However, only 8% of herds utilized this biosecurity measure. It is worth noting that none of the 9 closed beef suckler herds were seropositive for BVDV, whereas 13 of the 29 closed dairy herds (45%) were seropositive for BVDV.

Table 4.3: Univariate analysis of risks for BVDV seropositivity associated with movement biosecurity measures in open (a) beef suckler herds and (b) dairy herds.

Variable	Level	Cases	Controls	OR	95% CI	p-value
(a) Beef suckler herds						
Accredited herds	No	50	138	Ref	-	-
	Yes	37	15	1.12	0.55 – 2.18	0.747
Diagnostic screening	No	58	141	Ref	-	-
	Yes	7	34	0.50	0.19 – 1.13	0.119
Isolation period	No	19	40	Ref	-	-
	Yes	46	135	0.72	0.38 – 1.38	0.309
(b) Dairy herds						
Accredited herds	No	89	36	Ref	-	-
	Yes	17	14	0.49	0.21 – 1.11	0.084
Diagnostic screening	No	102	42	Ref	-	-
	Yes	4	8	0.21	0.05 – 0.69	0.013
Isolation period	No	67	27	Ref	-	-
	Yes	39	23	0.68	0.34 – 1.36	0.274

Farmers that thought their herd was currently affected by BVDV were no more or less likely implement at least one movement biosecurity measure than farmers that thought their cattle were unaffected by BVDV (OR: 0.87, 95 % CI: 0.38 - 2.11, p = 0.740 for beef suckler herds and OR:0.66, 95% CI: 0.26 – 1.61, p = 0.360 for dairy herds). Approximately 34% of beef suckler farmers and 26% of dairy farmers that believed their cattle were affected by BVDV sold animals as replacement breeding stock. Farmers that believed their herd was affected by BVDV were no less likely to sell replacement breeding stock than farmers that

thought their herd was unaffected (OR: 1.12, 95 % CI: 0.56 - 2.19, p = 0.745 for beef suckler herds and OR: 1.24, 95% CI: 0.46 – 3.31, p = 0.660 for dairy herds).

Biosecurity for local spread

Amongst all surveyed herds, 77.5% of beef suckler herds and 67.2% of dairy herds implemented at least one biosecurity measure to prevent disease transmission through local spread. There was no significant association between the total number of farms within a 10 km radius and the likelihood of farms implementing at least one biosecurity measure for either beef suckler herds (OR: 0.51, 95% CI: 0.15 – 1.51, p = 0.244) or dairy herds (OR: 1.36, 95% CI: 0.35 – 5.22, p = 0.652). None of the biosecurity measures significantly decreased the risk of herds being seropositive for BVDV in the univariate analyses (Table 4.4).

Table 4.4: Univariate analysis of risks for BVDV seropositivity associated with biosecurity measures against local spread in open (a) beef suckler herds and (b) dairy herds.

Variable	Level	Cases	Controls	OR	95% CI	p-value
(a) Beef suckler herds						
Double fencing fields	No	44	109	Ref	-	-
	Yes	21	75	0.69	0.38 – 1.25	0.230
Restricting visitor access	No	45	126	Ref	-	-
	Yes	20	58	0.97	0.52 – 1.76	0.910
Enforcing disinfection	No	39	116	Ref	-	-
	Yes	26	68	1.14	0.63 – 2.02	0.664
Separate vehicle drop-off	No	39	110	Ref	-	-
	Yes	26	74	0.99	0.55 – 1.76	0.975
(b) Dairy herds						
Double fencing fields	No	97	47	Ref	-	-
	Yes	22	19	0.56	0.28 – 1.14	0.108
Restricting visitor access	No	62	41	Ref	-	-
	Yes	57	25	1.51	0.82 – 2.81	0.190
Enforcing disinfection	No	75	41	Ref	-	-
	Yes	44	25	0.96	0.52 – 1.80	0.903
Separate vehicle drop-off	No	108	57	Ref	-	-
	Yes	11	9	0.65	0.25 – 1.69	0.359

Farmers that thought their herd was currently affected by BVDV were no more or less likely to implement at least one biosecurity measure against local spread than farmers that thought their cattle were unaffected by BVDV (OR: 1.59, 95 % CI: 0.71 – 3.95, p = 0.281 for beef suckler herds and OR:0.76, 95% CI: 0.31 – 1.89, p = 0.551 for dairy herds).

Discussion

The study findings highlight that many of the challenges experienced by other countries undergoing BVDV eradication are also likely to impact disease control efforts in Scotland. Current legislation is aimed at preventing disease transmission through cattle movements by requiring farmers to declare the infection status of their herd prior to any sales. Thus potential buyers will have the option of sourcing cattle directly from accredited disease-free herds or alternatively implementing appropriate quarantine and testing measures for cattle purchased from high risk herds. However, the relative importance of local spread compared to cattle movements, the low voluntary utilization of biosecurity measures amongst Scottish farmers, and the unproven efficacy of biosecurity measures as implemented by farmers in the field may potentially lead to significant delays in any reduction of BVDV prevalence. This paper has explored the existing evidence through the combination of available survey data (recording true herd status, existing management data, and farmer beliefs) with cattle movements.

In the multivariate logistic regression models, the combined cattle movement variables explained approximately 3 times more residual deviance than the combined local spread variables for beef suckler herds, but only 0.78 times as much residual deviance as the combined local spread variables for dairy herds. These findings are supported by the relative effect sizes observed in the univariate analyses of risk factors associated with seropositivity. Based on cattle demographics and herd management practices, there are several possible explanations for why local

spread is comparatively more important for the Scottish dairy industry than for the Scottish beef industry. Dairy production is highly concentrated in the lowland and south western regions of Scotland and the density of farms within a 10km radius was significantly higher than for beef suckler herds. Work by Ersbøll and colleagues (2010) showed that dairy herds in Denmark were more likely to become PI herds as the density of neighbouring farms with PI animals increased. A variety of transmission mechanisms have been implicated in local spread, including direct fence-line contact, airborne transmission, and the local movements of personnel, equipment, and wildlife (Mars et al., 1999; Niskanen and Lindberg, 2003). Dairy cattle are also managed much more intensively than beef cattle and the higher frequency of veterinarians, artificial insemination technicians, hoof trimmers, milk tankers, feed trucks, and other professionals entering farms may significantly increase the probability of spread through simple mass action effects alone (Bates et al., 2001; Brennan et al., 2008).

It was also shown that dairy herds purchased significantly fewer replacement breeding cattle and/or store cattle than beef suckler herds in the three year period prior to sampling with a greater percentage of herds remaining completely closed to cattle movements. As suggested by Caldow and colleagues (2005), it may be more economical for beef suckler herds with fewer than 150 breeding dams to purchase replacement heifers rather than maintain separate herds for breeding replacement stock and store cattle. However, empirical risk factor analyses have consistently shown that purchasing PI replacement heifers and cows carrying PI calves is associated with an increased risk of disease introductions, particularly since there are no available prenatal tests to determine the infection status of the foetus (Bitsch et al., 2000; Fray et al., 2000; Alban et al., 2001). Although the percentage of pregnant replacement dams was virtually the same for beef suckler and dairy herds, most dairy calves are removed from their dams within 24 hours of birth, which may decrease the risk of spreading disease to susceptible breeding cattle (Ezanno et al., 2008).

Differences in sampling frameworks for beef suckler and dairy herds also cannot be ruled out as possible explanations for the observed epidemiological differences. Seropositivity in beef suckler herds was determined by measuring the prevalence of BVDV antibodies amongst eligible young stock between 6 and 16 months of age. This is most likely to indicate recent BVDV exposure (Tråvén et al., 1991; Wentink et al., 1991; Mars et al., 1999; Niskansen et al., 2000), especially if disease was introduced through store cattle purchased for fattening. It is worth noting that the majority of beef suckler herds were sampled shortly after the autumn peak in between-herd store cattle movements. In contrast, seropositivity in dairy herds was determined by measuring BVDV antibody levels in bulk milk tank samples, which can remain elevated for months to years after PI cattle have been removed from the herd through either self-clearance or direct intervention (Niskanen, 1993; Ståhl et al., 2008). Given that movement patterns often change substantially from year to year, one might expect a weaker relationship between recent cattle movements and seropositivity in herds with a long-standing history of BVDV. Risk factors for local spread, such as shared ponds or the presence of sheep enterprises, are likely to be more consistent over time. However, this could not be evaluated with the available data. Being a non-experimental study, there also remains the possibility that the association was due to confounding with other variables and that there is no causal relationship.

Regardless of the timing and origin of exposure, there was evidence that biosecurity measures had limited ability to prevent BVDV transmission through movements or local spread. Part of the problem may stem from the questionnaire design. Farmers were only allowed to respond with simple yes or no answers, which inherently fail to capture heterogeneity in farmer behaviour. For example, approximately 20% of beef suckler and dairy farmers stated that they only sourced cattle from BVDV accredited herds. However, given the relatively small number of accredited herds selling cattle in Scotland relative to the volume of cattle trade, it is unlikely that farmers can source all of their animals exclusively from disease-free

herds. This may continue to be a problem for Scottish farmers if a large number of herds are classified as high risk under the new annual testing regime.

Performing diagnostic screening of animals at the time of purchase was a protective factor against seropositivity for dairy herds, but not for beef suckler herds. Evidence of a weak negative relationship between the total number of cattle movements and likelihood of an open herd implementing at least one biosecurity measure suggests that there may be significant financial and logistical constraints associated with testing and quarantining large numbers of purchased cattle (Heffernan et al., 2008). Although quarantine can be useful in allowing animals with transient infections to recover before co-mingling with susceptible breeding cattle, using quarantine as the sole biosecurity measure is unlikely to be effective in preventing the introduction of asymptomatic PI animals or dams carrying PI calves (Lindberg and Alenius, 1999). Only 20% of the beef suckler herds and 17% of the dairy herds in the study sample that reported using isolation periods also performed diagnostic screening. No information was available to assess how well the purchased animals were actually isolated from susceptible breeding cattle. The similar lack of efficacy for the biosecurity measures against local spread highlights the need for better farmer education and follow-up from veterinarians to ensure that recommendations are being implemented appropriately.

Studies from other regions undergoing BVDV eradication have reported difficulties in achieving good farmer compliance with biosecurity recommendations, especially when the recommendations are thought to be too costly or ineffective (Bitsch et al., 2000; Hult and Lindberg, 2005; Lindberg et al., 2006; Truyers et al., 2010). Only 28% of beef suckler farmers and 24% of dairy farmers with seropositive herds thought their cattle were affected by BVDV and those that did perceive a problem were no less likely to sell animals as replacement breeding stock and no more likely to implement biosecurity measures to prevent disease transmission through local spread than farmers with no perceived BVDV problems. Part of this effect may attributable to the phrasing of the survey question, which did

not clearly distinguish whether farmers thought their cattle were "affected" or "infected" with BVDV. It is possible that some farmers may have been aware that BVDV was present in the herd, but did not think it was affecting their cattle. These findings are important from a disease control perspective as farmers may not be willing to invest in disease control if the herd is not experiencing any significant reproductive losses or if there is a high risk of disease being introduced from neighbouring herds (Smith and Grotelueschen, 2004). Even if participation is not absolute, there can still be significant reductions in disease prevalence. For example, only 25% of herds in Styria, Austria participated in voluntary BVDV eradication programme, yet the overall risk of BVDV infection was reduced to a fifth of the original value after 30 months (Obritzhauser et al., 2005). The success of the eradication scheme was attributed to targeting important transmission pathways, which included the movements of PI cattle to seasonal grazing pastures. The increasing availability of data from the annual herd surveillance scheme will allow much more detailed risk factor analyses for Scotland.

Conclusion

The success of the current Scottish BVDV eradication programme may be undermined by spread through local transmission pathways and poor farmer compliance with biosecurity recommendations. The particular concern is the continued trade of PI cattle or cattle sold pregnant potentially with PI foetuses despite source herds being aware of positive BVDV status and purchasers being aware of the true source herd status. Changes in disease prevalence and farmer behaviour must be monitored closely over the next few years to determine whether additional legislation is needed to bring BVDV under control. Given the differences in BVDV epidemiology between beef suckler and dairy herds, it may be beneficial to develop greater differentiation in control programmes for each industry sector.

Chapter 5

Associations between bovine viral diarrhoea virus seropositivity and herd performance indicators[2]

Summary

Data from 255 Scottish beef suckler herds and 189 Scottish dairy herds surveyed as part of national bovine viral diarrhoea virus (BVDV) prevalence studies from October 2006 to May 2008 were studied retrospectively to determine the relationship between serological status and key performance benchmarks derived from national cattle movement records. On average, calf mortality rates were 1.35 percentage points higher in seropositive beef herds and 3.05 percentage points higher in seropositive dairy herds than in negative control herds. Seropositive beef herds were also more likely to show increases in calf mortality rates and culling rates between successive years. There were no discernible effects of BVDV on the average age at first calving or calving interval for either herd type. Accompanying questionnaire data revealed that only 27% of beef farmers and 25% of dairy farmers with seropositive herds thought their cattle were affected by BVDV, which suggests that the clinical effects of exposure may be inapparent under field conditions or masked by other causes of reproductive failure and culling. Beef farmers were significantly more likely to perceive a problem when their herd experienced acute changes in calf mortality rates, culling rates, and calving intervals between successive years. However, only 35% of these perceived positive herds were actually seropositive for BVDV. These findings emphasize both the importance of routinely screening herds to determine their true infection status and the potential for

[2] This chapter is a modified version of the following publication: Gates, M.C., Humphry, R.W., Gunn, G.J. Associations between bovine viral diarrhoea virus (BVDV) seropositivity and performance indicators in beef suckler and dairy herds. The Veterinary Journal (In press)

using national cattle movement records to identify herds that may be experiencing outbreaks from BVDV or other infectious diseases that impact herd performance.

Introduction

Bovine viral diarrhoea virus (BVDV) is an endemic cattle pathogen that causes significant economic losses for the beef and dairy industries through its effects on animal health and performance (Fray et al., 2000; Gunn et al., 2003). Cattle that become transiently infected close to breeding may have reduced conception rates (McGowan et al., 1993), while those infected during early gestation are at increased risk of pregnancy loss from early embryonic death and abortion (McClurkin et al., 1984; Houe, 1995). Foetal infections arising from the vertical transmission of BVDV in early gestation may result in the birth of persistently infected (PI) calves that shed large quantities of virus for life (McClurkin et al., 1984; Houe, 1995). Although some PI calves appear clinically normal and survive to enter the breeding herd (McClurkin et al., 1979; Muñoz-Zanzi et al., 2003; Bachofen et al., 2010), the majority are culled early due to poor growth performance, health complications secondary to immunosuppression, and the development of fatal mucosal disease (Houe, 1992, 1993). Higher mortality rates have also been reported amongst calves that are born weak or with congenital malformations following exposure to BVDV during late gestation (Kahrs et al., 1970).

Both empirical and theoretical studies have shown that prenatal infections account for a high proportion of financial losses incurred during a typical BVDV outbreak (Meyling et al., 1990; Valle et al., 2005; Varo Barbudo et al., 2008; Weldegebriel et al., 2009). However, the actual extent to which BVDV impacts herd performance under field conditions is highly variable and depends on complex factors such as the herd demographic structure at the time of disease introduction, the demographic characteristics of the index case, and the biosecurity practices in

place to prevent on-farm transmission (Moerman et al., 1994; Rüfenacht et al., 2001; Valle et al., 2001). This has two important implications from a disease control perspective. First, if the clinical signs of BVDV in transiently infected cattle are mild and non-specific, famers may not be aware that their herd is experiencing a problem with BVDV or they may attribute the changes in performance to other non-infectious causes of reproductive failure and calf mortality (Lindberg et al., 2006). Second, even if farmers are aware that BVDV is present in the herd, they may not perceive any benefits to controlling disease if there are no demonstrable effects on herd performance or if losses are expected to diminish over the course of outbreak due the development of herd immunity (Smith and Grotelueschen, 2004). In both cases, these herds remain at risk of spreading disease to other cattle herds through movements or local transmission mechanisms (Alban et al., 2001; Ersbøll et al., 2010).

The detailed records stored in national cattle movement databases provide a unique opportunity to study the effects of BVDV on herd performance. Based on the epidemiological features of the disease, it might be expected that herds with unusually high average ages at first calving or prolonged intervals between successive calvings may be experiencing pregnancy losses due to prenatal infections, while those with unusually high calf mortality rates may be experiencing the direct loss of persistently infected cattle. In this analysis, records from the Cattle Tracing System (CTS) database of Great Britain were used to investigate the relationship between BVDV seropositivity and several key measures of herd performance (calf mortality rates, average age at first calving, calving interval, and culling rates) in 255 Scottish beef suckler herds and 189 Scottish dairy herds that were surveyed from October 2006 to May 2008 as part of national seroprevalence studies. Information from the accompanying farm management surveys was also available to help assess how changes in herd performance over time may influence farmer perceptions of herd BVDV status. The results were used to highlight the

potential opportunities and limitations in using national cattle movement databases to identifying herds that may be experiencing BVDV outbreaks.

Methods

Study herds

A survey of 301 beef suckler herds was performed between October 2006 and September 2007 to estimate the prevalence of BVDV in the Scottish beef industry (Brulisauer et al., 2010). During the farm visit, blood samples were taken from approximately 10 randomly selected cattle between 6 and 16 months of age and processed using an indirect BVDV antibody ELISA to obtain antibody titres. For the purpose of this analysis, the 225 herds with little serological evidence of active infection in young stock were considered negative control herds and the remaining 76 herds with a within-group prevalence of more than 26.3%, (based on the two higher mixture distributions described previously for these data (Brulisauer et al., 2010)) were considered case herds. Herd owners or managers were also required to complete a management survey, which included questions on whether they thought their cattle were affected by BVDV.

A survey of 374 dairy herds was performed between October 2007 and May 2008 to estimate the prevalence of BVDV in the Scottish dairy industry (Humphry et al., 2012). Bulk milk tank samples were obtained directly through the farm's milk purchaser at the time of collection and processed using an indirect BVDV antibody ELISA to obtain the percentage positivity (PP) scores. Farmers were also required to complete a management survey similar to the one used in the beef study. Herds that were routinely vaccinated for BVDV were identified and removed from subsequent analyses due to the potential for interference with the bulk milk tank serology results (Houe et al., 2006). Within the questionnaire, farmers were also surveyed as to whether or not they thought their cattle were affected by BVDV. Based on the Swedish BVDV eradication class system, the remaining 220

unvaccinated herds were assigned into one of four groups based on their PP score. Class 0 herds were considered unlikely to have any seropositive animals indicating a low probability of BVDV infection, while Class 3 herds were considered highly likely to have many seropositive animals indicating a recent or active infection. For the purpose of this analysis, the 77 herds designated as Class 0 or Class 1 were considered negative control herds and the remaining 143 herds designated as Class 2 or Class 3 were considered BVDV seropositive case herds.

Cattle movement data

The Cattle Tracing System (CTS) database contains virtually complete records of all births, deaths, and movements of individual cattle in Great Britain since January 2001(Green and Kao, 2007), which can be used to generate key benchmarks of herd performance (Caldow et al., 2005). Records for an individual herd can be accessed through its unique county-parish-holding (CPH) number. The original beef and dairy management data contained only information on the farm business name and main farm address and so to link the serological results from the study herds with the corresponding cattle movement data, attempts were made to match this information against a database of CPH codes provided by the Scottish government. Farms for which there was no available CPH code or for which there was an obvious discrepancy between the survey estimates of herd size and CTS database estimates of herd size were excluded. These were most likely herds where the cattle were housed on a different location than the main farm business. The final study sample contained 255 beef suckler herds (67 case herds and 188 control herds) and 189 dairy herds (122 case herds and 67 control herds).

All birth records from each study herd during the two year period prior to sampling were extracted from the Livestock Movements table and linked to demographic records from other CTS data tables to generate the following calving event information: calf birth date, calf death date, calf death location (abattoir or agricultural holding), dam birth date, dam death date, and when applicable, the date

and location of any previous or subsequent calvings. Records from 240 of the 86,358 calving events (0.28%) with missing or inaccurate information were discarded. These included dams that were identified as being male, dams that were not located on the farm associated with the calf birth record at the time of calving, dams that were less than 19 months of age at the time of calving, and dams where the recorded birth date, calving date, and death date were not in chronological order.

Performance indicators

The basic calving event records were used to generate the following performance variables: calf mortality rate, average age at first calving, culling rate, and calving interval. The calf mortality rate was calculated as the percentage of all calves born during the specified time period that died on an agricultural holding within 365 days of birth. It was assumed that calves slaughtered at an abattoir were intended for the veal production market and therefore excluded from the mortality calculations. The average age at first calving was calculated as the difference between the date of birth and the date at calving, in months, for all heifers that calved on the farm during the specified time period. A heifer was defined as an animal between 19 and 48 months of age with no previously recorded calving dates in the CTS database. The purpose for placing restrictions on age was to eliminate potential outliers that may have been caused by data entry errors or animals that may have delivered an unrecorded stillborn calf at an appropriate age. The culling rate was calculated as the percentage of dams that calved during the specified time period that were subsequently slaughtered or sold within 365 days of calving. The calving interval was calculated as the number of months between successive calving dates for the subset of dams that delivered another calf within 24 months. It was assumed that in most production herds, any animals that failed to deliver a calf within 24 months would be culled from the herd and outlying values were most likely attributable to data entry errors and unrecorded births, stillbirths, or abortions.

The performance variables were calculated both as an average over the entire two year period and then individually for each year within the two year time period. The purpose was to assess whether BVDV serological status and farmer perceptions of BVDV serological status were associated with acute changes in herd performance as well as general differences in the level of herd performance. The change in performance between years was expressed as the absolute difference between the value reported for the first year and the value reported for the second year.

Statistical analyses

Data for the beef suckler herds and dairy herds were analysed separately due to inherent difference in management practices as well as differences in the sampling methodology used to assess seropositivity. For each herd type, two separate analyses were performed. The first analysis explored differences in performance between seropositive and negative control herds to evaluate the potential for using cattle movement records to identify affected herds. Given the importance of calf mortality, the percentage of calf deaths attributable to the herd BVDV status (population attributable risk) was calculated using the univariate odds ratio in Levin's formula (Bruzzi et al., 1985). The second analysis explored differences in performance between herds that were perceived to be affected by BVDV and herds that were perceived to have no problems with BVDV to determine whether poor performance or changes in performance were associated with farmer perceptions.

The mean and percentile distributions (10^{th}, 50^{th}, and 90^{th}) for each performance variable were reported. Based on visual assessment of the variable distributions, comparisons between case and control herds were made using Mann-Whitney U tests for the two year averaged performance variables and Student's t tests for the variables describing the change in performance between years. The cut-off value for statistical significance was set at $p < 0.05$. Multivariate logistic regression models were also constructed for the beef suckler herds to test the

potential interactions between performance variables. However, as none of the variables reached significance in combination, the results are not presented here. For dairy herds, there were not enough significant associations in the univariate comparisons to warrant further multivariate analysis.

Results

Descriptive univariate statistics on the performance of beef suckler herds and dairy herds by serological status are presented in Table 5.1 and Table 5.2, respectively. The average calf mortality rate was 1.35 percentage points higher in seropositive beef suckler herds and 3.05 percentage points higher in seropositive dairy herds. However, the overall population attributable risk of calf mortality associated with BVD seropositivity was only 7.85% for beef suckler herds and 14.3% for dairy herds. Seropositive beef suckler herds were also found to have significant increases in calf mortality rates and culling rates between successive years compared to the control herds. There were no significant differences in the average age at first calving, calving interval, and culling rates for either herd production type.

Table 5.1: Comparison of performance indicators between BVD seropositive beef suckler herds and control herds.

		Percentiles			
	Mean	10th	50th	90th	p-value
Seropositive herds (N = 67)					
Calf mortality rate (%)	4.79	1.27	3.81	9.51	0.003
Age at first calving (months)	31.7	26.3	32.3	36.6	0.848
Culling rate (%)	16.6	5.47	13.3	25.0	0.271
Calving interval (months)	12.9	12.3	12.7	13.5	0.202
Change in calf mortality rate (%)	1.38	-3.11	0.85	5.41	0.040
Change in age at first calving (months)	-0.53	-5.28	-0.54	4.52	0.827
Change in culling rate (%)	6.52	-7.52	1.10	29.5	0.011
Change in calving interval (months)	0.05	-0.61	-0.04	0.89	0.598
Control herds (N = 188)					
Calf mortality rate (%)	3.44	0.00	3.11	6.82	
Age at first calving (months)	32.5	27.6	32.6	37.2	
Culling rate (%)	13.8	6.08	11.0	23.1	
Calving interval (months)	12.8	12.2	12.7	13.5	
Change in calf mortality rate (%)	0.21	-4.82	0.00	4.74	
Change in age at first calving (months)	0.13	-4.75	-0.26	4.44	
Change in culling rate (%)	0.27	-11.4	0.91	13.9	
Change in calving interval (months)	0.07	-0.76	-0.01	1.01	

Table 5.2: Comparison of performance indicators between BVD seropositive dairy herds and control herds.

		Percentiles			
	Mean	10th	50th	90th	p-value
Seropositive herds (N = 122)					
Calf mortality rate (%)	9.48	2.17	8.46	17.7	0.001
Age at first calving (months)	34.1	30.5	33.7	38.1	0.215
Culling rate (%)	20.9	12.3	20.3	29.2	0.236
Calving interval (months)	13.9	13.1	13.8	15.1	0.574
Change in calf mortality rate (%)	0.04	-7.67	-0.12	6.38	0.457
Change in age at first calving (months)	0.16	-2.79	0.09	3.49	0.627
Change in culling rate (%)	-1.54	-11.4	-0.79	9.50	0.752
Change in calving interval (months)	-0.08	-0.89	-0.09	0.81	0.394
Control herds (N = 67)					
Calf mortality rate (%)	6.43	1.56	5.66	11.9	
Age at first calving (months)	33.6	29.2	33.6	38.6	
Culling rate (%)	19.5	10.6	19.8	29.0	
Calving interval (months)	13.9	13.0	13.8	14.6	
Change in calf mortality rate (%)	-0.04	-5.76	0.34	5.35	
Change in age at first calving (months)	0.27	-2.14	0.43	2.73	
Change in culling rate (%)	-0.57	-10.9	-0.56	6.78	
Change in calving interval (months)	-0.11	-0.98	-0.18	0.76	

Only 27.2% of beef suckler farmers and 24.5% of dairy farmers with seropositive herds thought their cattle were affected by BVDV (Table 5.3). Of the herds that were thought to be affected by BVDV, 64.8% of beef suckler herds and 14.3% dairy herds were classified as seronegative at the time of sampling.

Table 5.3: Descriptive statistics on the farmer perception of herd BVDV status and the true serological status of (a) beef suckler herds and (b) dairy herds.

(a) Beef suckler		Serological status		(b) Dairy		Serological status	
		+	–			+	–
Farmer perception	Affected	18	33	Farmer perception	Affected	30	5
	Unaffected	35	112		Unaffected	33	25
	Don't know	13	40		Don't know	59	37

There was no significant difference in the absolute indicators of performance in beef suckler and dairy that were perceived to be infected with BVDV compared to those that were perceived to be unaffected by BVDV over the two year study period (Table 5.4). However, beef suckler herds that experienced acute increases in the calf mortality rates, culling rates, and calving intervals between successive years and dairy herds that experienced acute increases in the calf mortality rate between successive years were significantly more likely to be perceived as being affected by BVDV.

Table 5.4: Comparison of performance indicators between beef suckler herds perceived to be affected by BVDV and beef suckler herds perceived to be unaffected by BVDV.

		Percentiles			
	Mean	**10th**	**50th**	**90th**	**p-value**
Perceived to be affected (N = 57)					
Calf mortality rate (%)	3.97	0.00	3.16	9.43	0.807
Age at first calving (months)	32.1	27.1	31.9	36.7	0.680
Culling rate (%)	18.4	8.54	11.8	35.1	0.056
Calving interval (months)	12.8	12.1	12.7	13.5	0.698
Change in calf mortality rate (%)	1.62	-4.26	1.14	5.89	0.048
Change in age at first calving (months)	0.46	-3.55	0.55	4.25	0.116
Change in culling rate (%)	8.67	-9.50	3.06	34.9	0.005
Change in calving interval (months)	0.26	-0.30	0.30	1.25	0.014
Perceived to be unaffected (N = 147)					
Calf mortality rate (%)	4.06	0.79	3.76	7.48	
Age at first calving (months)	32.4	27.1	32.5	37.2	
Culling rate (%)	13.8	5.92	11.3	22.8	
Calving interval (months)	12.8	12.2	12.7	13.6	
Change in calf mortality rate (%)	0.40	-4.78	0.00	5.06	
Change in age at first calving (months)	-0.42	-4.73	-0.55	4.12	
Change in culling rate (%)	-0.21	-10.1	0.77	11.5	
Change in calving interval (months)	0.01	-0.73	-0.07	0.93	

Table 5.5: Comparison of performance indicators between dairy herds perceived to be affected by BVDV and dairy herds perceived to be unaffected by BVDV.

		Percentiles			
	Mean	10th	50th	90th	p- value
Perceived to be affected (N = 35)					
Calf mortality rate (%)	9.43	2.42	7.74	15.6	0.222
Age at first calving (months)	33.8	30.7	33.9	37.8	0.229
Culling rate (%)	20.4	13.0	20.2	25.3	0.448
Calving interval (months)	13.9	13.2	13.8	15.0	0.371
Change in calf mortality rate (%)	1.69	-4.99	1.49	6.71	0.011
Change in age at first calving (months)	0.18	-2.84	0.23	3.26	0.594
Change in culling rate (%)	-1.54	-12.1	-0.54	6.46	0.876
Change in calving interval (months)	-0.12	-0.74	-0.16	0.42	0.560
Perceived to be unaffected (N = 58)					
Calf mortality rate (%)	8.56	3.01	7.17	17.0	
Age at first calving (months)	33.5	29.2	33.2	38.8	
Culling rate (%)	19.9	11.6	20.3	27.0	
Calving interval (months)	13.8	12.9	13.8	14.5	
Change in calf mortality rate (%)	-0.90	-7.21	-0.37	4.61	
Change in age at first calving (months)	0.29	-2.08	0.38	2.80	
Change in culling rate (%)	0.42	-7.35	-0.33	11.2	
Change in calving interval (months)	-0.10	-0.92	-0.11	0.89	

Discussion

Findings from this analysis highlight that the performance of beef suckler and dairy herds is highly variable under field conditions and only partially explained by the presence of BVDV. Similar to other comparative empirical studies, it was found that calf mortality rates in seropositive herds were approximately 1 to 3 percentage points higher on average than those reported in negative control herds (Ersbøll et al., 2003; Diéguez et al., 2009). While some of this increase may be directly attributable to the birth of PI calves and calves with congenital abnormalities following foetal infections with BVDV (Rüfenacht et al., 2001), it is

important to note that only a small fraction of calf deaths overall were attributable to the herd serological status. Other factors such as the incidence of twinning and dystocias, nutritional management of breeding dams, seasonal variation in calving patterns, and general calf husbandry practices, are also likely contributing to mortality in these herds (Wells et al., 1996; Mee et al., 2008). Another possible explanation is that herds that are at increased risk of introducing BVDV are also at increased risk of introducing other infectious diseases with the potential to increase calf mortality rates (Ortiz-Pelaez and Pfeiffer, 2008; Stott and Gunn, 2008).

There were no apparent differences in the average age at first calving, culling rates, and calving intervals between seropositive herds and negative control herds. Variable effects have been reported elsewhere in the literature. In a study of Norwegian dairy herds, Valle and colleagues (2001) found, for example, that BVDV status had no significant effect on the average calving interval, but was associated with an increased risk of culling across all age groups of animals. In contrast, Niskanen and colleagues (1995) found that the average calving interval in Swedish dairy herds with high bulk milk tank antibody levels was increased by approximately 9 days, but that there was no significant effect of BVDV status on culling rates. While some of the discrepancy may be linked to regional differences in farm management, these findings also emphasize that the clinical effects of BVDV may be inapparent or masked by other common causes of reproductive failure such as bull infertility, artificial insemination technique, and post-partum management (Grohn and Rajala-Schultz, 2000; McDougall, 2006). There are few published studies available on beef suckler herds for comparison. However, it has been reported that spring calving herds in the United States with at least one PI animal have approximately 5% fewer dams in calf at the fall pregnancy examination (Wittum et al., 2001).

Another significant finding was that seropositive beef suckler herds were more likely to have an increase in culling rates between successive years compared

to negative control herds. This result is not surprising given that poor fertility is one of the main reasons why animals are culled from the breeding herd (McDermott et al., 1992; Bascom and Young, 1998) as well as one of the main clinical sequelae of acute BVDV infections (McGowan et al., 1993; Fray et al., 2000). With most beef suckler herds restricting their breeding seasons to a narrow time window, farmers will often choose to cull animals that fail to conceive or lose the pregnancy rather than incur the additional maintenance costs of retaining them for future breeding (Lesmeister et al., 1973). These culling decisions may further mask the effects of BVDV on the average age at first and calving interval (Valle et al., 2001), which is an important, but not yet widely recognized reason why BVDV outbreaks often go unnoticed by farmers and veterinarians.

One of the main limitations in this study was the lack of information on when and how disease was first introduced to the herd. As empirical and theoretical studies have shown, this can have a significant impact on the severity and duration of BVDV outbreaks (Sprecher et al., 1991; Viet et al., 2004; Ezanno et al., 2007). For example, if susceptible dams were exposed to BVDV prior to the start of breeding or outside of the gestational risk period for generating PI calves, there may not have been any apparent reproductive losses from reduced fertility or abortions. Additionally, in herds where the disease has become endemic, there may be sufficient levels of immunity to prevent further reproductive losses (Innocent et al., 1997). The latter provides an alternate explanation as to why many farmers with seropositive herds did not perceive problems with BVDV in their cattle. Other researchers have suggested that farmers may not perceive problems simply because they are unaware of what normal performance should be for their herds (Brownlie et al., 2011).

Similar to Sarrazin and colleagues (2013), the results suggested that most farmers were unaware of the true disease status of their herds, although interestingly, farmers were more likely to perceive a problem if there were acute changes in

performance between successive years. This has several important implications from a disease control perspective. First, under the new BVDV eradication scheme in Scotland, all farmers must test their cattle every year and declare the infection status of their herd to any potential buyers (Anonymous, 2013). This will ensure that farmers with seropositive herds are aware of their herd's status and farmers with disease free herds can take appropriate biosecurity measures to prevent disease introductions. Second, if farmers with seropositive herds are not experiencing detectable reproductive losses, they may not perceive any benefits to controlling BVDV (Billinis et al., 2005) and additional legislation may be required to prevent these herds from transmitting disease through cattle movements or local spread (Bitsch et al., 2000). Third, the significant associations between performance and perceptions suggest that farmers with disease free herds may be attributing acute changes in calf mortality and culling rates to BVDV rather than other potentially significant infectious and non-infectious causes. Monitoring spatial and temporal trends in herd performance using national animal health databases may allow earlier identification of BVDV outbreaks as well as other infectious disease incursions (Carpenter et al., 2007; Perrin et al., 2012).

Another limitation in the present study was in the sampling methods used to determine herd serological status. In beef suckler herds, seropositivity was assessed by measuring the prevalence of BVDV antibodies amongst eligible young stock. If disease was only recently introduced through the purchase of infected store cattle for fattening, there may have not have been sufficient time for disease to spread and cause reproductive problems in the breeding herd (Tråvén et al., 1991; Wentink et al., 1991; Mars et al., 1999; Niskansen et al., 2000). It is worth noting that the majority of beef suckler herds were sampled immediately following the autumn peak in store and fattening cattle movements. It is also possible that cattle with persistent maternal antibodies were incorrectly classified as being positive for BVDV. However, due to the low expected prevalence of these animals in the 6 to 16 month

old age group (Palfi et al., 1993) and the use of finite mixture modelling to classify the overall herd as being seropositive or negative, this is unlikely to have introduced any significant bias to the analysis (Brulisauer et al., 2010). In dairy herds, seropositivity was assessed by measuring BVDV antibody levels in bulk milk tank samples, which can remain elevated for months to years after PI cattle have been removed from the herd through self-clearance or direct intervention (Niskanen, 1993; Ståhl et al., 2008; Booth et al., 2013). Where there is no ongoing exposure to BVDV, herd performance would be expected to return to baseline levels (Fredriksen et al., 1998).

The measure of whether a herd had been vaccinated for BVDV was a single binary response to the question 'Do you routinely vaccinate your herd for BVD?' This firstly does not account for variation in the number of cattle vaccinated, which groups are vaccinated, and how recently cattle have been vaccinated all of which are likely to be important in affecting antibody levels in blood or bulk milk. Secondly, the ability to determine the herd's vaccination status depends on the herd owners or managers providing accurate and consistent answers to the question. Evidence from Nespeca and colleagues (1997) suggests that farmer responses to biosecurity questions on surveys do not always reflect biosecurity practices on the farm and it cannot be ruled out that some of the study herds may have been misclassified as seropositive for BVDV.

The availability of detailed demographic information in the CTS database provided a unique opportunity to retrospectively analyze the relationship between seropositivity and performance in the surveyed beef suckler and dairy herds. However, the CTS database was originally intended for use in slaughter traceback investigations and several challenges were encountered in using the records to generate indicators of herd performance. First, farmers are not required to report the births of stillborn calves or calves that die within several hours of birth. A recent survey of dairy herds in southern England estimated that 7.9% of calves fall into

these two categories (Brickell et al., 2009), which may lead to underestimation of the calf mortality rates and overestimation of the age at first calving and calving intervals. Given that BVDV can contribute to perinatal mortality, this bias is likely to affect seropositive herds disproportionately more than seronegative herds. It was also not possible to distinguish calves that were slaughtered within the first year of life for veal production from those that were slaughtered due to poor performance. Although this may again underestimate the true impact of BVDV on calf mortality, the findings that on-farm mortality rates were higher in seropositive herds than seronegative herds are still robust. Additional bias may have been introduced through the exclusion of farms that could not be linked to their CTS records through the main farm business address. However, as there is no obvious reason why these unmatched farms would have a different prevalence of BVDV, this is unlikely to have affected the main study findings. This does, however, highlight the importance of collecting accurate and detailed information on farm identification in future survey studies to enable the integration of risk factor variables from diverse data sources.

Conclusion

The extent to which BVDV impacts herd performance is highly variable under field conditions and as a result, many farmers with seropositive herds may be unaware that their cattle are affected by BVDV or unwilling to invest in disease control measures. Findings from this analysis support the new legislative requirements in Scotland that all cattle breeding herds must be tested for BVDV annually and declare the infection status of their herds to potential buyers so that appropriate biosecurity measures can be taken. For regions without mandatory BVDV screening, monitoring changes in calf mortality rates and culling rates using records stored in national cattle movement databases may be useful in identifying herds experiencing outbreaks with BVDV or other infectious disease that impact

herd performance. More generally, these findings reinforce the substantial epidemiological benefits that can be achieved by combining routinely collected cattle movement data with detailed serology and questionnaire data from active surveillance projects.

Chapter 6

Cascade effects of herd performance on industry level disease transmission dynamics

Summary

Farms that purchase replacement breeding cattle have an increased risk of introducing many economically important livestock diseases. The objectives of this analysis were to determine whether the total number of replacement breeding cattle purchased by individual farms could be reduced by improving herd reproductive management and to quantify the effects of such reductions on the industry-level transmission dynamics of endemic cattle diseases. Detailed information on the reproductive performance and contact patterns of British cattle herds was extracted from the national cattle movement database for use in the study models. In a given calendar year, approximately 65% of beef herds and 55% of dairy herds purchased at least one replacement breeding animal. Results from zero-inflated negative binomial (ZINB) regression models revealed that herds with high average ages at first calving, prolonged calving intervals, abnormally high or low culling rates, and high calf mortality rates were significantly more likely to be open herds and to purchase greater numbers of replacement breeding cattle over a three year period. If all beef and dairy herds achieved the same level of performance as the top 20% of herds, the total number of replacement breeding cattle purchased could be reduced by an estimated 34% and 42%, respectively. At the industry level, only 13% of batch movements in the contact network contained replacement breeding cattle. However, these movements had a disproportionately strong influence on disease transmission dynamics due to their greater betweenness centrality. For a disease similar to bovine viral diarrhoea virus, removing all replacement breeding cattle movements resulted in a 46% reduction in endemic prevalence compared to a 19% reduction when movements were eliminated at random. As a disease control strategy, improving reproductive management may be particularly effective because

of its ability to target multiple pathogens simultaneously while having easily demonstrable effects on farm profitability.

Introduction

Beef and dairy herds require a constant supply of replacement breeding cattle to maintain or increase herd size. A key decision facing producers is whether to raise heifers internally for replacement or to purchase replacement breeding cattle directly from outside sources (Van Arendonk, 1985). The optimal strategy for any given herd depends on a number of complex factors including land and labour availability, cash flow needs, market prices, and future business goals (Gartner, 1981; Groenendaal et al., 2004). Heifers require intensive management and nutritional support to reach an appropriate physical maturity by the target age at first breeding (Le Cozler et al., 2008) and for farms that cannot provide this cost-effectively, there can be significant financial advantages to breeding calves with desirable growth and carcass characteristics for fattening instead (Roughsedge et al., 2003; Dal Zotto et al., 2009). Due to the long production cycle of cattle, farms that are undergoing rapid expansion to capture favourable market prices may also choose to purchase replacement cattle rather than rely on internal growth (Aadland, 2004).

In some cases, however, the decision to purchase replacement cattle is directly determined by herd reproductive performance. Farms that cull excessive numbers of animals for infertility, poor performance, and other health related issues have an increased demand for replacement breeding cattle (Hadley et al., 2006), while farms with high calf mortality rates, delayed ages at first calving, and prolonged calving intervals may not have an adequate supply of heifers to meet replacement needs (Bascom and Young, 1998; Grohn and Rajala-Schultz, 2000). As numerous empirical studies have shown, these farms are not only losing significant profit through reduced productivity (Britt, 1985; Grohn and Rajala-Schultz, 2000), but also increasing their risk of introducing many economically important cattle

diseases such as contagious mastitis (Garcia Alvarez et al., 2011), bovine viral diarrhoea virus (Tinsley et al., 2012), bovine tuberculosis (Gilbert et al., 2005), bovine paratuberculosis (Woodbine et al., 2009b), and bovine herpesvirus type-1 (Woodbine et al., 2009a). Since the movements of replacement breeding cattle form part of a larger contact network, there may be cascade effects on the industry level transmission dynamics for many of these endemic cattle diseases.

Although the basic structure of cattle movement networks has been well described (Bigras-Poulin et al., 2006; Natale et al., 2009; Volkova et al., 2010), little is currently known about the extent or epidemiological impact of replacement breeding cattle trade. In this analysis, data from the national cattle movement database in Great Britain is used to characterize the reproductive performance and movement patterns of cattle breeding herds. Zero-inflated negative binomial regression models were used to determine the association between herd reproductive management and the number of replacement breeding cattle purchased by beef and dairy herds. The effects of removing replacement breeding cattle movements from the contact network on the transmission dynamics of endemic pathogens were evaluated with simple disease simulation models. The results are used to emphasize that the management decisions of individual herds can have a substantial impact on the epidemiology of infectious disease at the industry level.

Methods

Cattle movement data

The Cattle Tracing System (CTS) database contains virtually complete demographic and movement records for individual cattle present in Great Britain since January 2001. This includes information on date of birth, birth location, date of death, death location, sex, breed classification (beef, dairy, or dual breed), and the unique CTS livestock identification number of calves that survived parturition. The latter can be used to generate key reproductive performance indicators for breeding

dams such as the age at first calving, interval between successive calvings, and gestational stage at any given time. Movements on or off cattle locations are recorded with information on the departure location, destination location, movement date, and movement type (birth, death, or movement).

The subsequent analyses used data from January 2004 through December 2006 to characterize patterns in replacement breeding cattle trade and herd reproductive performance. The primary reason for selecting this time period was to ensure that sufficient pre- and post-movement data was available to classify animals into production groups. It was assumed that animals intended for human consumption would be slaughtered by 30 months of age to comply with bovine spongiform encephalopathy (BSE) regulations and animals intended for breeding would deliver their first calf by 48 months of age. At the time of this study, CTS data was available through April 2010.

For the purpose of this analysis, a farm was defined as any location with a unique county-parish-holding (CPH) number that was classified as an agricultural holding or landless keeper (farmer raising cattle on rented land) in the CTS database.

Reproductive management variables

There were 8,415,283 recorded calvings on 67,868 farm locations in Great Britain from January 2004 through December 2006. This analysis focused on the subset of 33,404 farms with at least 20 beef and/or 20 dairy cattle births per year. This included 19,340 exclusively beef farms, 14,064 exclusively dairy farms, and 571 mixed production farms. Altogether these herds accounted for 83.5% of the total number of calvings in Great Britain. Beef herds and dairy herds managed on mixed production farms were treated as separate units in the remaining analyses. The main reasons for restricting the sample were to eliminate small scale operations where cattle breeding was unlikely to be the primary source of farm income (Ezanno et al., 2006) and to eliminate farms that may have been in the process of entering or exiting the cattle industry.

For each calving event, the following information was recorded: calving farm, calving date, dam date of birth, dam breed classification, date and location of any previous or subsequent calvings, date of the next recorded movement off the calving farm, calf breed classification, calf sex, and calf date and location of death. The basic calving event records were aggregated by farm to generate the following reproductive performance variables: average age at first calving, calving interval, culling rate, calf mortality rate.

The average age at first calving was calculated as the difference between the age at calving and date of birth in months for all heifers that calved on the farm during the specified time period. A heifer was defined as an animal between 19 and 48 months of age with no previously recorded calving dates in the CTS database. The purpose for placing restrictions on age was to eliminate potential outliers that may have been caused by data entry errors or animals that may have delivered an unrecorded stillborn calf at an appropriate age. The calving interval was calculated as the number of months between successive calving dates for the subset of dams that delivered another calf within 730 days. It was assumed that in most production herds, any animals that failed to deliver a calf within 24 months would be culled from the herd and outlying values were most likely attributable to data entry errors or unrecorded births. The culling rate was calculated as the percentage of calvings where the dam was subsequently slaughtered or sold within 500 days of calving. The calf mortality rate was calculated as the percentage of all calves born during the specified time period that died on an agricultural holding within 365 days of birth. It was assumed that calves slaughtered at an abattoir were intended for the veal production market and therefore excluded from the mortality calculations. All variables were averaged over the three year study period.

Three additional variables were created to describe other reproductive management decisions. The average number of calvings per year was used as an estimate of herd size. The absolute change in the number of calvings from 2004 to 2006 was used to identify herds that were undergoing expansion and reduction. The

percentage of heifers slaughtered at an abattoir by 30 months of age was used as an indication of heifers that were unsuitable as breeding replacements. This included animals that were bred as fattening cattle and animals that were culled for poor conformation or infertility. The total number of replacement breeding cattle purchased over the three year period was also recorded from the cattle movement records.

Reproductive management analysis

Zero-inflated negative binomial (ZINB) regression models were used to explore the relationship between herd reproductive management and the purchase of replacement breeding cattle. Data for beef suckler herds and dairy herds were analyzed separately due to inherent difference in management practices. The logistic component of the ZINB model provided insight on factors influencing the odds of herds remaining closed over the three year study period, while the negative binomial component provided insight on factors influencing the expected count of replacement cattle purchased over the three year study period. Prior to analysis, a logarithmic transformation (base 10) was applied to herd size and the reproductive performance variables (change in herd size, percentage of heifers culled by 40 months of age, age at first calving, calving, interval, and calf mortality rate) were divided into categories by quintile. For culling rate, the reference category was set at 15 – 20% for beef herds and 25 – 35% for dairy herds based on the industry target values (Youngquist and Threllfall, 1997) and an additional two levels above and below the reference category were created using cut-off values that produced groups of approximately equal size.

A preliminary univariate screen was performed to identify variables that were associated with dependent variable at a p-value < 0.20 for inclusion in the final models. All variables were retained in both the logistic and negative binomial components of the final multivariate models based on their statistical significance at the $p < 0.05$ level. The Vuong test statistic was used to confirm the choice of a zero-

inflated model over standard negative binomial regression. For the logistic components of the models, odds ratios (ORs) and 95% confidence intervals were reported. The coefficients and standard errors (SEs) were reported for the negative binomial components of the models. All statistical analyses were performed in R (R-Development-Core-Team, 2010).

The equations from the final ZINB regression models were then used to predict the effects of improving herd reproductive performance on the total number of replacement breeding cattle purchased by beef and dairy herds. As a baseline for comparison, the empirically observed values for reproductive in the model equations were first used to estimate the total number of replacement breeding cattle purchased. Then, each of independent variables (with the exception of herd size) was set to a target value and the new predicted values for the total number of replacement breeding cattle purchased were calculated. For age at first calving, calving interval, and calf mortality variables, the target value was set as the top quintiles. For change in herd size, all herds that underwent expansion were set to the middle category representing no growth. For the percentage of heifers, farms in the bottom four quintiles were each moved up one level and for culling rate, the target value was set as the reference category representing the industry target value. The results were expressed as the percentage reduction in the total number of purchased replacement from the baseline value. Each variable was tested alone and in combination.

Movement network

There were a total of 7,917,890 individual movements between cattle farms in the period from January 2004 through December 2006. Similar to previous studies, movements that occurred through a livestock market were treated as a single direct movement from the original departure herd to the final destination herd after sale (Vernon and Keeling, 2009; Volkova et al., 2010). Animals were classified into production groups based on their demographic characteristics at the time of

movement. A breeding heifer was defined as a female animal with no recorded calvings that either subsequently delivered a calf or survived beyond 30 months of age. A breeding cow was defined as a female animal with at least one recorded calving prior to the movement date. All animals that were less than 280 days from the next recorded calving date were considered pregnant. Beef breed cows that were moved onto the farm at the same time as their calf and dairy breed cows that were within 305 days of the previous recorded calving date were considered to be in lactation. The remaining movements included store calves, fattening cattle, breeding bulls, and replacement heifers that were culled before breeding.

For the purpose of this analysis, a replacement breeding heifer was defined as an animal that was born on a different location that the destination farm and subsequently calved on the destination farm, while a replacement breeding cow was defined as an animal that previously calved on a different location than the destination farm and subsequently calved on the destination farm. These definitions were used to distinguish true cattle sales from temporary movements between seasonal grazing pastures, movements between locations operated by the same cattle business, and movements through farms acting livestock dealers. Approximately 1% of individual movement records were discarded due to missing or inaccurate information. Detailed descriptive statistics on the frequency and characteristics of replacement breeding cattle movements were provided for the study herds based on data from 2005.

Network transmission dynamics

The effect of removing replacement breeding cattle movements from the contact network on disease transmission dynamics was evaluated with a simple SIS simulation model. First, the cattle movement network was reconstructed by aggregating the individual movement records from 01 January 2004 through 31 December 2006 into batch movement records such that all cattle moving from farm A to farm B on the same date were considered a single batch movement. This

resulted in a network with 2,695,402 batch movements between 90,478 unique farm locations. All batch movements that contained at least one replacement breeding female were subsequently classified as replacement breeding cattle movements.

At the beginning of each simulation, disease was seeded on 10,000 farms at random on 01 January 2004. Each affected farm was assigned an infectious period drawn at random from an exponential distribution with a half-life, *h* (Tinsley et al., 2012). The model was then updated in time steps of one day. If an infected farm moved a batch of cattle to a susceptible farm, there was a fixed probability, *p*, that the destination farm would also become infected. The probability was not weighted according to the number of cattle moved. Farms that reached the end of their infectious period reverted back to a susceptible state. To ensure adequate time for the system to reach steady state equilibrium, the simulation was allowed to run for a total of 50 years by recycling the 3 year movement data set. Endemic prevalence was measured as the average number of farms infected on any given day over the last 3 years of the simulation. The simulation code was implemented in the C programming language.

In the first set of simulation scenario, *h* was set at 1,085 days and *p* was set at 0.05 to approximate the transmission dynamics of a pathogen similar to bovine viral diarrhoea virus (Tinsley et al., 2012). A targeted removal approach was used to assess the relative importance of replacement breeding cattle movements to network transmission dynamics (Rautureau et al., 2010). At the beginning of each simulation, a proportion of replacement breeding cattle movements were removed from the network data set at random. The simulation was then run on the reduced movement network to monitor changes in the predicted endemic prevalence. A total of 10,000 simulations were performed with the proportion to be removed drawn at random from a uniform distribution bounded at 0 and 1 representing no removal and complete removal, respectively. As a benchmark for comparison, another 10,000 simulations were performed where an equivalent number of movements were removed from the network at random. The results from both simulation sets were

plotted as the percentage of total network movements removed against the percentage change in endemic prevalence using the maximum recorded value for endemic prevalence amongst the simulations as the baseline value.

In the second set of simulation scenarios, the proportion of replacement breeding cattle movements removed from the network was fixed at 1, but the values for *h* and *p* were varied in each replicate to determine whether the observed effects were consistent across for broader range of endemic pathogens. At the beginning of each simulation, the value for *h* was drawn from a uniform distribution ranging from 90 days to 1,825 days and the value for *p* was drawn from a uniform distribution ranging from 0.01 to 0.25. A total of 100,000 simulations were performed. Similar to the first scenario, another 100,000 simulations were performed removing the equivalent number of movements at random for comparison. The results were again expressed as the additional percentage change in endemic prevalence relative to the baseline simulations with random elimination of movement edges.

Based on results from the simulation models, the edge betweenness centrality of replacement breeding cattle movements and the node betweenness centrality of farms that purchased replacement breeding cattle were also calculated using the igraph library for in the C programming environment (Csardi and Nepusz, 2006). Edge betweenness centrality measures the number times a movement falls on the shortest path between pairs of farms, while node betweenness centrality measures the number of shortest paths between pairs of farms in the network that pass through a particular farm.

Results

Descriptive statistics

There were 19,340 beef herds and 14,635 dairy herds with at least 20 recorded calvings in the CTS database during the 2005 calendar year. Descriptive statistics on their demographic characteristics are summarized in Table 6.1. The

average beef herd had 57 calvings (median: 41, range: 20 to 1,503), while the average dairy herd had 92 calvings (median: 76, range: 20 to 1,093). An estimated 65.2% of beef herds were open, 28.4% were closed, and 6.3% had no replacement animals calve in the herd. Open beef herds purchased an average of 9.3 replacement animals (median: 5, range: 1 to 429) from an average of 4.44 source herds (median: 3, range: 1 to 112). In contrast, an estimated 55.3% of dairy herds were open, 43.2% were closed, and 1.5% had no replacement animals calve in the herd. Open dairy herds purchased an average 14.3 replacement animals (median: 8, range: 1 to 550) from an average of 5.3 herds (median: 3, range: 1 to 152). For open herds of both production types, there was wide variation in the proportion of replacement animals that were purchased rather than home raised. In total, 15.1% of all beef herds and 5.5% of all dairy herds chose to replace their culled animals exclusively with purchased cattle.

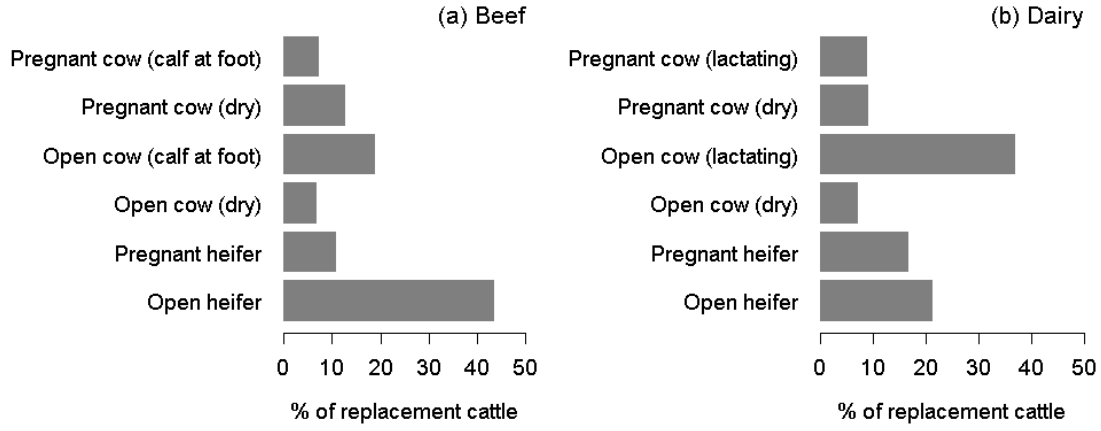
Table 6.1: Descriptive statistics on the demographic characteristics of British (a) beef and (b) dairy herds with at least 20 recorded calvings in 2005.

			Percentiles		
	Mean	SD	10th	50th	90th
(a) Beef					
Open herds					
Herd size	62	58.3	23	45	116
% replacement cattle in herd	21.8	16.6	6.9	17.8	40.7
% of replacements purchased	73.9	30.4	22.5	87.5	100
Number purchased	9.3	13.2	1	5	21
Number of source herds	4.4	5.4	1	3	10
Closed herds					
Herd size	51	42.1	22	38	93
% replacement cattle in herd	15.2	11.4	4.0	13.1	27.4
(b) Dairy					
Open herds					
Herd size	99	72.2	35	81	179
% replacement cattle in herd	31.7	14.9	15.8	30.0	46.9
% of replacements purchased	46.6	34.1	6.3	38.8	100
Number purchased	14.3	22.3	1	8	33
Number of source herds	5.3	6.9	1	3	12
Closed herds					
Herd size	86	55.2	32	73	153
% replacement cattle in herd	24.7	11.1	12.0	24.2	37.1

The overall percentage of beef and dairy herds that purchased replacement breeding cattle was relatively consistent between the three study years (65.7%, 65.2%, and 60.3% for beef and 55.4%, 55.3%, and 53.5% for dairy). Amongst the beef herds, 45.8% purchased replacement breeding cattle in all three years, 20.3% purchased cattle in two years, 13.7% purchased cattle in one year, and 20.8% remained completely closed. Amongst the dairy herds, 41.3% purchased replacement breeding cattle in all three years, 14.3% purchased cattle in two years, 11.5% purchased cattle in one year, and 32.8% remained completely closed. For herds that consistently purchased replacement breeding cattle, there was only moderate correlation in the total numbers purchased between years ($r = 0.49$ for beef and $r = 0.62$ for dairy, $p < 0.001$ for both).

Distributions of the types of replacement animals purchased by open beef and dairy herds are shown in Figure 6.1. Open heifers were the most commonly purchased replacement animal for beef herds at 43.3%. A total of 26.1% of purchased beef cows were sold with a calf at foot. For dairy herds, open lactating cows were the most common type of purchased replacement animal at 36.8%.

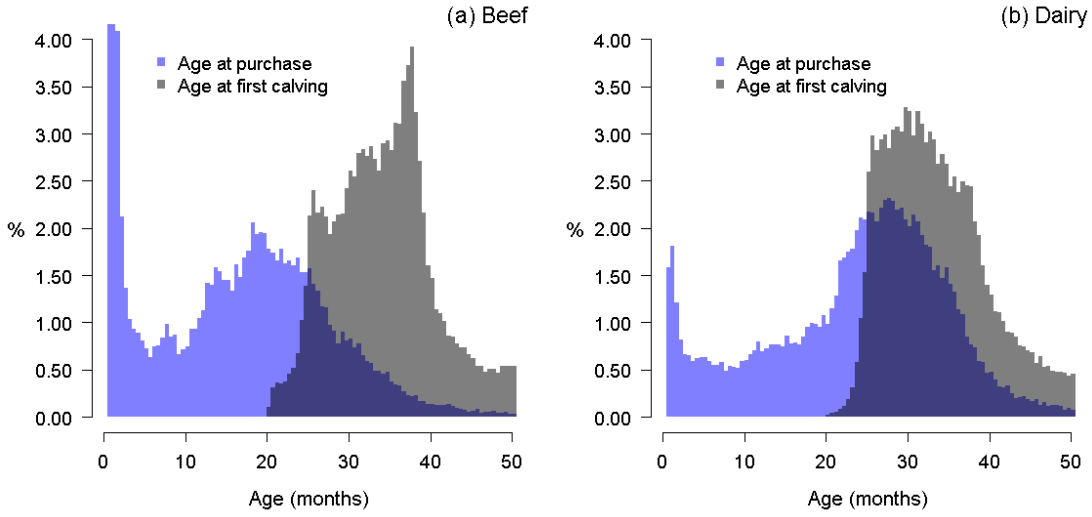
Figure 6.1: Distribution of the production type of replacement animals purchased by British (a) beef and (b) dairy herds in 2005.



Overall, 46.7% of beef heifers and 14.8% of dairy heifers that calved in 2005 were purchased as replacement animals. Figure 6.2 shows the age distribution of

heifers at the time of purchase relative to the distribution of ages at first calving. For beef cattle, there were large peaks in the purchase of heifers shortly after birth and approximately every 6 months thereafter. The majority of beef replacement heifers were also purchased in advance of their first calving season. For dairy cattle, there was a large peak in replacement cattle movements at approximately 30 months of age corresponding with the average age at first calving for the dairy industry. Purchased beef replacement heifers were approximately 2 weeks older at the time of calving than home-raised heifers, while purchased dairy heifers were approximately 6 weeks older.

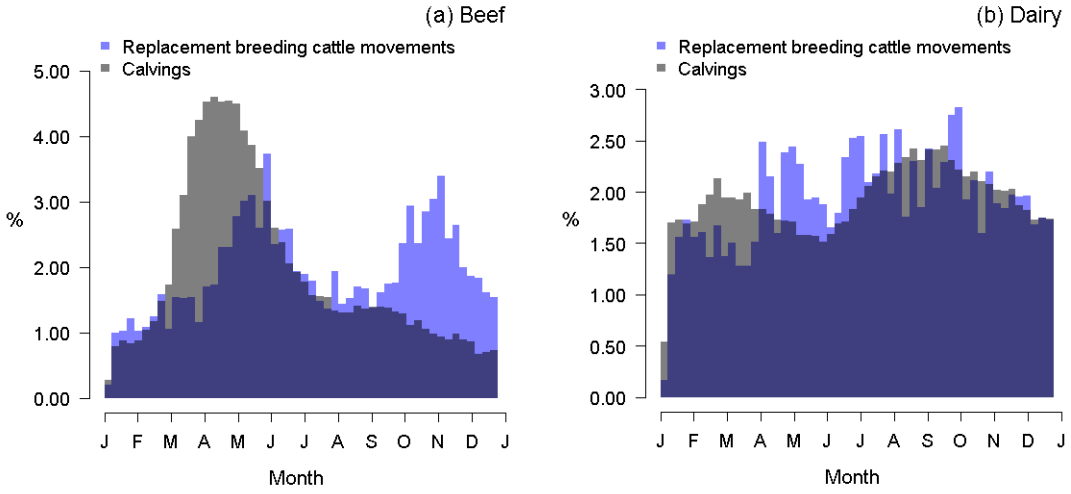
Figure 6.2: Age distribution of replacement breeding heifers at the time of purchase and average age at first calving for (a) beef breed cattle and (b) dairy breed cattle. Note the x axes have been truncated at 50 months.



The movements of purchased replacement breeding heifers and cows accounted for 12.3% of all individual between-herd cattle movements in Great Britain from 01 January 2005 through 31 December 2005. Of these, 30.9% occurred through a livestock market and 69.1% occurred directly from farm to farm. There was a strong seasonality to the movements of replacement beef cattle corresponding to the strong seasonality of calvings in the British beef industry (Figure 6.3a). The

distributions of movements and calvings were more uniform across the year for dairy cattle (Figure 6.3b).

Figure 6.3: Seasonal distribution of replacement breeding cattle movements and calvings for (a) beef and (b) dairy dams in 2005.



Descriptive statistics on the reproductive performance of the study herds from 2004 through 2006 are summarized in Table 6.2. For both production types, there were approximately as many herds undergoing expansion in size as there were herds undergoing reduction in size. On average, 56.4% of heifers born in beef herds and 33.2% of heifers born in dairy herds died or were slaughtered by 30 months of age without ever having calved. The average age at first calving was approximately 32.8 months for both beef and dairy herds. Fewer than 2.5% of all beef and dairy herds achieved an average calving interval less than the target of 365 days. An estimated 23.1% of beef herds had culling rates within the target range of 15 to 20% and an estimated 25.4% of dairy herds had culling rates within the target range of 25 to 35%. The average calf mortality rate for dairy herds (6.69%) was more than twice as high as the average calf mortality rate for beef herds (2.66%). There were significant differences between herds in the top and bottom deciles for each reproductive performance variable.

Table 6.2: Descriptive statistics on the reproductive management of British (a) beef and (b) dairy herds over the 2004 to 2006 period

			Percentiles		
	Mean	SD	10th	50th	90th
(a) Beef herds					
Change in herd size (%)	17.8	247	- 31.8	- 1.7	45.7
Heifers culled by 30 months (%)	56.4	17.8	31.5	59.0	76.8
Age at first calving (months)	32.7	3.89	27.6	32.8	37.2
Calving interval (days)	395	23.3	373	390	425
Culling rate (%)	17.9	12.2	7.1	15.1	31.7
Calf mortality rate (%)	2.66	2.70	0.00	1.96	5.97
(b) Dairy herds					
Change in herd size (%)	- 0.79	98.6	- 39.3	- 3.30	28.1
Heifers culled by 30 months (%)	33.2	17.2	12.6	30.8	57.8
Age at first calving (months)	32.8	3.61	28.4	32.6	37.3
Calving interval (days)	426	22.8	399	424	455
Culling rate (%)	27.6	15.1	14.7	23.6	48.2
Calf mortality rate (%)	6.69	4.92	1.78	5.66	12.7

Reproductive management

The ZINB models for beef and dairy herds revealed many significant associations between herd reproductive management and the risk of purchasing replacement breeding cattle (Table 6.3 and Table 6.4). The Vuong tests for beef ($V = 25.7$, $p < 0.001$) and dairy ($V = 26.2$, $p < 0.001$) herds had high positive values indicating that the zero-inflated models fit the data better than standard negative binomial regression.

In the logistic component of the models, the odds of a beef or dairy herd being closed decreased significantly as the herd size, change in herd size, and percentage of heifers culled by 30 months of age increased. Beef herds with average ages at first calving in the second and third quintiles (29.5 to 31.8 months and 31.8 to 33.8 months, respectively) were significantly less likely to be closed than herds in the top quintile (< 29.5 months), while herds in the bottom quintile (> 35.8 months) were significantly more likely to be closed. Similar trends with the average age at

first calving were observed for dairy herds. In general, as the average calving interval and calf mortality rates increased, the odds of a herd being closed decreased. However, the trends were appreciably stronger for dairy herds than for beef herds. Beef and dairy herds with culling rates above or below the industry target range were also more likely to be closed.

In the negative binomial component of the models, the total number of replacement breeding cattle purchased by beef and dairy herds generally increased with herd size, change in herd size, percentage of heifers culled by 30 months of age, calving interval, culling rate, and calf mortality rate. For dairy herds, there was also an increase in the number of replacement breeding cattle purchased as the average age at first calving increased. This trend was not observed for beef herds.

Table 6.3: Results from the (a) logistic and (b) negative binomial components of the zero-inflated negative binomial regression model predicting the likelihood of being a closed herd and the number of replacement breeding cattle purchased by beef herds, respectively.

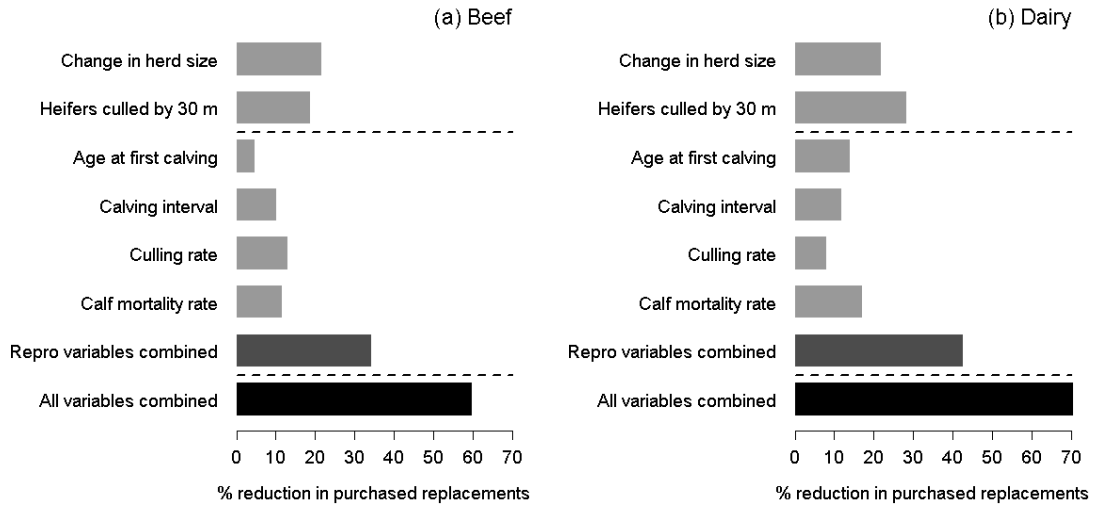
		(a) logistic			(b) negative binomial		
Variable	**Levels**	**OR**	**95% CI**	**p-value**	**Coeff**	**SE**	**p-value**
$\log_{10}$(herd size)	–	0.58	0.49 – 0.69	< 0.001	2.103	0.031	< 0.001
Change in herd size (%)	< -20	1.64	1.42 – 1.89	< 0.001	- 0.327	0.028	< 0.001
	-20 to -5	1.18	1.04 – 1.89	0.013	- 0.171	0.025	< 0.001
	-5 to + 5	Ref	-	-	Ref	-	-
	5 to 20	0.83	0.72 – 0.96	0.013	0.159	0.027	< 0.001
	> 20	0.60	0.52 – 0.69	< 0.001	0.746	0.026	< 0.001
Heifers culled by 30 months of age (%)	< 42	Ref	-	-	Ref	-	-
	42 to 55	0.63	0.57 – 0.71	< 0.001	0.175	0.028	< 0.001
	55 to 63	0.30	0.27 – 0.35	< 0.001	0.352	0.028	< 0.001
	63 to 71	0.20	0.17 – 0.23	< 0.001	0.554	0.028	< 0.001
	> 71	0.14	0.12 – 0.16	< 0.001	0.674	0.028	< 0.001
Average age at first calving (months)	< 29.5	Ref	-	-	Ref	-	-
	29.5 to 31.8	0.69	0.60 – 0.80	< 0.001	0.091	0.025	< 0.001
	31.8 to 33.8	0.71	0.62 – 0.82	< 0.001	0.086	0.025	0.001
	33.8 to 35.8	1.04	0.91 – 1.19	0.540	0.034	0.026	0.192
	> 35.8	1.32	1.17 – 1.50	< 0.001	- 0.072	0.027	0.007
Calving interval (days)	< 378	Ref	-	-	Ref	-	-
	378 to 386	0.83	0.73 – 0.95	0.007	0.034	0.025	0.176
	386 to 395	0.75	0.65 – 0.85	< 0.001	0.063	0.025	0.012
	395 to 410	0.71	0.62 – 0.81	< 0.001	0.113	0.026	< 0.001
	> 410	0.85	0.75 – 0.97	0.016	0.204	0.027	< 0.001
Culling rate (%)	< 10	1.73	1.51 – 1.97	< 0.001	- 0.381	0.026	< 0.001
	10 to 15	1.24	1.10 – 1.41	0.001	- 0.188	0.022	< 0.001
	15 to 20	Ref	-	-	Ref	-	-
	20 to 25	1.06	0.91 – 1.24	0.461	0.164	0.028	< 0.001
	> 25	1.17	1.02 – 1.36	0.029	0.582	0.026	< 0.001
Calf mortality rate (%)	< 0.62	Ref	-	-	Ref	-	-
	0.62 to 1.50	0.96	0.84 – 1.10	0.547	0.071	0.026	0.003
	1.50 to 2.53	0.90	0.79 – 1.03	0.134	0.078	0.026	< 0.001
	2.53 to 4.21	0.89	0.78 – 1.02	0.101	0.108	0.026	< 0.001
	> 4.21	0.86	0.75 – 0.99	0.037	0.215	0.026	< 0.001

Table 6.4: Results from the (a) logistic and (b) negative binomial components of the zero-inflated negative binomial regression model predicting the likelihood of being a closed herd and the number of replacement breeding cattle purchased by dairy herds, respectively.

		(a) logistic			(b) negative binomial		
Variable	**Levels**	**OR**	**95% CI**	**p-value**	**Coeff**	**SE**	**p-value**
$\log_{10}$(herd size)	–	0.65	0.55 – 0.78	< 0.001	1.940	0.045	< 0.001
Change in herd size (%)	< -20	1.30	1.13 – 1.49	< 0.001	-0.143	0.038	< 0.001
	-20 to -5	1.11	0.98 – 1.25	0.106	-0.019	0.035	0.597
	-5 to + 5	Ref	-	-	Ref	-	-
	5 to 20	0.86	0.76 – 0.98	0.021	0.225	0.037	< 0.001
	> 20	0.53	0.45 – 0.61	< 0.001	0.757	0.038	< 0.001
Heifers culled by 30 months of age (%)	< 18	Ref	-	-	Ref	-	-
	18 to 27	1.00	0.89 – 1.13	0.974	0.215	0.038	< 0.001
	27 to 35	0.85	0.75 – 0.96	0.009	0.459	0.038	< 0.001
	35 to 47	0.56	0.50 – 0.64	< 0.001	0.573	0.037	< 0.001
	> 47	0.19	0.16 – 0.22	< 0.001	1.026	0.037	< 0.001
Average age at first calving (months)	< 29.8	Ref	-	-	Ref	-	-
	29.8 to 31.7	0.78	0.69 – 0.89	< 0.001	0.103	0.035	0.003
	31.7 to 33.5	0.91	0.80 – 1.03	0.149	0.188	0.036	< 0.001
	33.5 to 35.6	1.04	0.91 – 1.18	0.564	0.175	0.037	< 0.001
	> 35.6	1.31	1.15 – 1.50	< 0.001	0.282	0.039	< 0.001
Calving interval (days)	< 407	Ref	-	-	Ref	-	-
	407 to 419	0.86	0.76 – 0.98	0.021	0.040	0.036	0.270
	419 to 429	0.83	0.73 – 0.94	0.004	0.030	0.036	0.407
	429 to 443	0.79	0.70 – 0.90	< 0.001	0.128	0.037	0.001
	> 443	0.74	0.65 – 0.84	< 0.001	0.223	0.037	< 0.001
Culling rate (%)	< 20	2.14	1.91 – 2.39	< 0.001	-0.656	0.031	< 0.001
	20 to 25	1.46	1.30 – 1.64	< 0.001	-0.314	0.031	< 0.001
	25 to 35	Ref	-	-	Ref	-	-
	35 to 40	1.12	0.90 – 1.39	0.326	0.307	0.056	< 0.001
	> 40	1.21	1.04 – 1.40	0.013	0.418	0.038	< 0.001
Calf mortality rate (%)	< 2.86	Ref	-	-	Ref	-	-
	2.86 to 4.68	0.88	0.78 – 1.00	0.050	-0.028	0.038	0.468
	4.68 to 6.71	0.79	0.70 – 0.90	< 0.001	0.094	0.038	0.013
	6.71 to 9.75	0.65	0.57 – 0.74	< 0.001	0.155	0.038	< 0.001
	> 9.75	0.57	0.50 – 0.65	< 0.001	0.201	0.019	< 0.001

The ZINB models were then used to predict the effects of altering herd reproductive management on the total number of replacement breeding cattle purchased by the study herds (Figure 6.4). Setting the change in herd size to no growth for herds undergoing expansion resulted in a 21.6% reduction in the total number of replacement breeding cattle purchased for beef and a 21.8% reduction for dairy. Reducing the percentage of heifers culled by 30 months of age by one quintile resulted in an 18.6% reduction for beef and a 28.4% reduction for dairy. Setting all the reproductive performance variables for each herds to the top quintile reduced the number of replacement breeding cattle purchased by 34.2% for beef and 42.4% for dairy. The maximum achievable reduction by altering all variables simultaneously was 59.8% for beef and 70.3% for dairy.

Figure 6.4: Percentage reduction in the predicted number of replacement breeding cattle purchased by (a) beef and (b) dairy herds by altering herd reproductive management

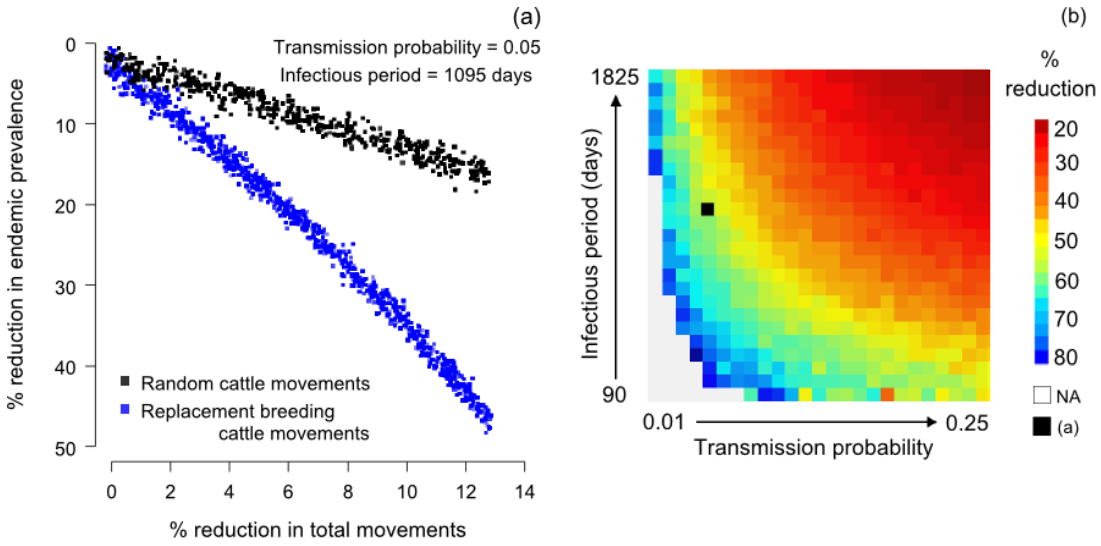


Network transmission dynamics

The simulation models revealed that replacement breeding cattle movements had a disproportionately strong influence on network transmission dynamics. At a transmission probability of 0.05 and infectious period half-life of 1,095 days,

removal of all replacement breeding cattle movements (13.3%) from the network resulted in an approximately 45.8% reduction in endemic prevalence (Figure 6.5a). Removal of the equivalent number of movements at random decreased endemic prevalence by only 19%. The effects of removing replacement breeding cattle movements compared to removing movements at random were more pronounced for diseases with low transmission probabilities and short infectious periods (Figure 6.5b).

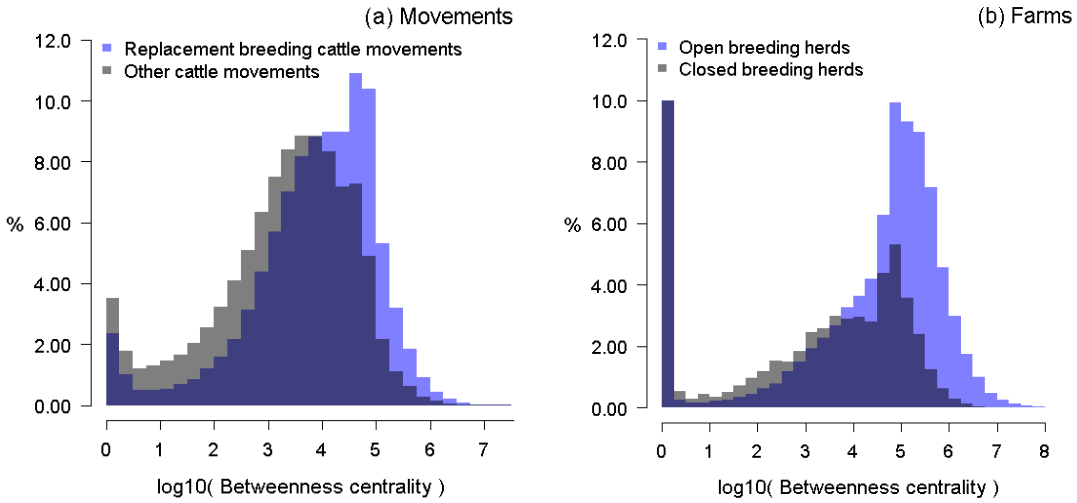
Figure 6.5: Estimated reduction in endemic prevalence from (a) the removal of varying proportions of replacement breeding cattle movements at a fixed transmission probability of 0.05 and an infectious period half-life of 1095 days and (b) the removal of all replacement breeding cattle movements with varying transmission probabilities and infectious period half-lives. The black square in (b) indicates the parameter combination shown in (a).



From a network perspective, the movements of replacement breeding animals had significantly higher betweenness centrality scores than the movements of other type cattle ($D = 0.193$, $p < 0.001$). The median log transformed betweenness centrality of replacement breeding cattle movements was 4.04 (range: 0 to 7.49) compared to 3.49 (range: 0 to 7.82) for other cattle movements. Correspondingly, open breeding herds were also more central in the network than

closed breeding herds. The distributions of movement and farm betweenness centrality scores are shown in Figure 6.6.

Figure 6.6: Relative betweenness centrality of (a) replacement breeding cattle movements compared to other cattle movements and (b) open breeding herds compared to closed breeding herds from 2005. Note the values for farms with a betweenness centrality of zero have been truncated from 23.4% for open herds and 55.6% for closed herds.



Discussion

Although many studies have used records from the CTS database to investigate the spread of disease through British cattle movement networks (Kao et al., 2006; Robinson et al., 2007; Vernon and Keeling, 2009; Volkova et al., 2010), this is the first to my knowledge that establishes a direct relationship between the management practices of individual herds and the theoretical risk of infectious disease transmission. The most significant finding in the present study was that herds with poor reproductive performance were not only losing profitability, but also contributing to the persistence of endemic diseases by purchasing excess numbers of replacement breeding cattle. Developing strategies that can reduce the herd-level demand for breeding replacements, increase the herd-level supply of replacement

heifers, and lower the costs of on-farm heifer rearing programmes represents a novel approach to controlling disease at the population level.

The CTS database was originally designed to trace the movement history and potential contacts of animals that tested positive for bovine spongiform encephalopathy at slaughter. As such, there are several limitations in using the data to generate statistics on herd reproductive performance and movement patterns that must be considered when interpreting the study findings. First, a breeding herd was defined as any location with a unique CPH number that had at least one recorded beef or dairy calving. Larger farm businesses may house cattle on several locations and with the available data, it was not possible to determine which of these locations were linked (Madders, 2006). Therefore, some of the animals classified as replacement breeding cattle or culled cattle may have been transfers within the same farm business rather than transfers of ownership. It was also assumed that dairy breeding cattle housed on the same location as beef breeding cattle were separate production units. However, these dairy cattle may have been strictly used to produce crossbreed calves for the beef production unit (Amer et al., 2001). Second, farmers are not required to register the births of stillborn calves or calves that died within several hours of birth. This may lead to underestimation of calf mortality rates and breeding herd size as well as overestimation of the average age at first calving and calving intervals. Finally, records in the CTS database are not free from error and a small proportion of calving records were discarded due to missing or biologically implausible data.

Descriptive statistics revealed that approximately 65% of beef herds and 55% of dairy herds purchased at least one replacement breeding animal during any given calendar year. Based on the results from farmer surveys, the majority of these animals were unlikely to have been tested, quarantined, or sourced from certified herds to prevent disease transmission (Faust et al., 2001; Brennan and Christley, 2012). Replacement breeding cattle were also commonly sold in small batches of one or two animals, which means that farmers must often source animals from

multiple herds to obtain the required number of replacements. This practice has been highlighted as a risk factor for spreading epidemics like foot-and-mouth disease (Green and Kao, 2007; Robinson and Christley, 2007) and is likely also important for increasing the herd level risk of acquiring endemic pathogens.

Contrary to expectations that larger herds would be able to raise replacement heifers more cost-effectively than smaller herds due to economies of scale (Caldow et al., 2005), the ZINB models revealed that both the odds of purchasing replacement breeding cattle and the total number of replacement breeding cattle purchased increased significantly with herd size. These findings may be partially attributed to ongoing changes in the demographics of British beef and dairy farming. With the rising costs of production and decreased support from agricultural subsidization, many smaller farms have chosen to exit the cattle industry while many larger farms have undergone rapid expansion to capture economies of scale (Dunne et al., 2001; Huettel and Jongeneel, 2011). The latter is most often accomplished by purchasing in large batches of replacement breeding cattle rather than waiting for several years to produce additional replacement heifers through internal growth. In this analysis, only 21.3% of beef herds and 26.2% of dairy herds that expanded by more than 20% remained completely closed.

Also contrary to expectations, the risk of purchasing replacement breeding cattle was less in herds with culling rates that were above or below the industry target ranges. It is possible that some of the herds with low culling rates were compensating for an inadequate supply of replacement heifers by retaining a greater percentage of mature breeding cattle, while some of the herds with high culling rates were in the process of exiting the cattle industry. A small number of herds in England and Wales may have been subject to movement restrictions and increased culling as part of bovine tuberculosis control efforts (Abernethy et al., 2013). Even through the risk of disease introductions was lower, herds that cull too few animals are losing opportunities to improve herd genetics and performance, while herds that cull too many animals are losing profitability through the costs of raising extra

replacement heifers to maintain herd size (Korver and Renkema, 1979; Heikkilä et al., 2008). The negative binomial portion of the ZINB models predicted that number of replacement breeding cattle increased with herd culling rates, which supports the hypothesis that herds with high culling rates have an increased demand for replacement cattle.

Poor fertility is one of the leading risk factors for culling amongst beef and dairy cattle (McDermott et al., 1992; Esselmont and Kossaibati, 1997). The prolonged calving intervals observed in the study herds suggest that many cattle are not becoming pregnant and delivering subsequent calves in a timely fashion. This limits the number of replacement heifers an animal produces over its lifespan, which increases both the risk of purchasing replacement cattle as well as the number of cattle purchased. The trends in risk with worsening performance were not as strong as expected. Several researchers have highlighted that calving intervals may be artificially low in herds that are culling excessive animals for poor fertility (Bourdon and Brinks, 1983; MacGregor and Casey, 1999). With more beef herds in Great Britain practicing seasonal calving, there is greater pressure to cull animals that fail to conceive within the narrow breeding window and so the potential bias is likely to have affected beef herds more than dairy. For the dairy industry, there is a well-established trade-off between high milk production and fertility that may constrain improvements in performance (Lucy, 2001; de Vries and Risco, 2005; Evans et al., 2006). However, the wide variation in performance between the top and bottom producing herds suggests that on-farm management factors also play a key role (Grohn and Rajala-Schultz, 2000).

For herds of both production types, the total number of replacement breeding cattle purchased increased with the mortality rate. Pre-weaning calf mortality has a direct impact on the supply of replacement heifers and it has been recommended that death losses should not exceed 5% (Youngquist and Threllfall, 1997). The majority of beef herds were well below this threshold, which may explain why the risk of being a closed herd decreased only marginally as the calf mortality rate increased.

In contrast, almost 60% of dairy herds had a mortality rate greater than 5%. This may be partly attributed to the fact that male dairy calves have a lower economic value and generally do not receive the same standard of care as replacement heifers (Lombard et al., 2007). Dairy calves are also separated from their dams shortly after birth and factors such as colostrum intake, housing conditions, nutritional management, and infectious disease control become even more critical in preventing calf deaths (Svensson et al., 2003; Wathes et al., 2008; Brickell et al., 2009).

The percentage of heifers culled by 30 months age provided a simple measure to evaluate the relative supply of heifers available as breeding replacements. A recent survey study by Wathes and colleagues (2008) estimated that only 68% of heifer calves born in dairy herds would survive to first lactation, which is consistent with this study's findings from the CTS database. Heifer culling rates were significantly higher in beef herds, but with the limited demographic information in the CTS database, it was not possible to determine whether these animals were intentionally bred for fattening or whether they were raised as replacement heifers, but culled involuntarily due to inadequate growth, poor conformation, or general infertility. The difference is important from a disease control perspective. For herds that cannot raise replacement breeding heifers cost-effectively under the farm resource constraints, there can be significant financial advantages to producing terminally bred or crossbred calves for fattening instead (Wolfova et al., 2005; Dal Zotto et al., 2009). However, if the high heifer culling rates are indicative of poor herd management, there is still the possibility of targeting these herds to reduce number of replacement breeding purchased. For example, dairy farmers in Great Britain will often use beef bulls to breed animals that fail to conceive through artificial insemination. Therefore, improving the efficiency of artificial insemination programmes may be an effective means of increasing the supply of heifers available for replacement.

The costs of raising replacement heifers represent a significant percentage of the total costs of beef and dairy production (Tozer and Heinrichs, 2001). As

numerous economic analyses have shown, maximum efficiency is achieved when heifers deliver their first calf by 24 months of age (Haworth et al., 2008; Wathes et al., 2008; Berry and Cromie, 2009). This is directly attributable to the reduced feed and maintenance costs as well as the increased productive lifespan of heifers that calve at an earlier age. Although it was found that the majority of beef and dairy herds in Great Britain were calving heifers closer to 33 months of age, the relationship between average age at first calving and the risk of purchasing replacement breeding cattle was complex. Compared to herds ranked in the top 20% for performance, those in second quintile were significantly more likely to be open, while those in the bottom quintile were significantly more likely to be closed. Part of this trend may related to the difficulty in ensuring that heifers have reached an appropriate physical maturity by the start of the breeding season or the target age at first calving for the herd. Heifers that are bred too young have a greater risk of calving complications (Funston and Deutscher, 2004), which can effect subsequent fertility and performance (Ettema and Santos, 2004). Consequently, farmers may choose to retain heifers for breeding in subsequent autumn or spring calving seasons (Hickson et al., 2010), which would increase the average age at first calving, but reduce the need to purchase animals from outside sources. For dairy herds, the total number of replacement breeding cattle purchased increased with the average age at first calving. However, this may be confounded by the fact that purchased replacement heifers were also significantly older at the time of calving than home-raised heifers.

The interpretation of the study findings is also complicated by the fact that poor reproductive performance can be both a cause and effect of purchasing replacement breeding cattle. For example, Thomsen and others (2006) found that culling rates were significantly higher in Danish dairy herds with a large proportion of purchased cows. It was suggested that herds with excessively high culling rates may not have an adequate supply of heifers to meet replacement needs thereby necessitating the purchase of replacement breeding cattle from outside sources.

However, herds that purchase replacement breeding cattle are at increased risk of introducing diseases like bovine viral diarrhoea virus (BVDV) and bovine herpesvirus type I (BHV I), which can in turn lead to increased culling through their effects on fertility and abortion (van Schaik et al., 1998; Rüfenacht et al., 2001; Valle et al., 2001; Tiwari et al., 2005). Similarly, high calf mortality rates may limit the availability of replacement heifers, but may also be linked to the presence of infectious diseases introduced through animal movements (Ersbøll et al., 2003; Raboisson et al., 2013).

Only 13.3% of all batch movements between herds contained at least one replacement breeding female and yet they had a disproportionately strong influence on network transmission dynamics due to their high betweenness centrality. This may again be related to marketing practices since herds that purchase replacement breeding cattle must often source animals from multiple herds, which increases the number of inward contacts. These farms may also be selling larger numbers of cattle for fattening, which increases the number of outward contacts. Both are important determinants of network centrality. Even if these movements cannot be prevented through targeted trade restrictions, it may possible to apply disease specific biosecurity measures such as quarantine, vaccination, or diagnostic testing to effectively remove them from the contact network (Natale et al., 2009; Natale et al., 2011; Rautureau et al., 2012). These measures may be more effective against some pathogens than other. It was also shown that the magnitude of the observed effect decreased as both the farm infectious period and movement transmission probability were increased. Other researchers have similarly shown that the structural and temporal features of cattle movement networks matter less for diseases that spread over long time periods (Kao et al., 2007) or have a higher probability of spreading through batch movements (Vernon and Keeling, 2009).

The simulation study used a simplistic disease transmission model that considered all farms to be homogenous production units regardless of their size or demographic structure and all movements to carry the same risk of transmitting

disease regardless of the number or production type of cattle moved. While these assumptions may be appropriate for highly infectious epidemic diseases that spread rapidly and indiscriminately between herds, endemic pathogens often have unique epidemiological features that can modify transmission risk (Carslake et al., 2011). For example, factors such as age, gender, and production type can influence the probability of purchased cattle being infected as well as their probability of being commingled directly susceptible production groups in the receiving herd (Ezanno et al., 2008). The rate of disease clearance from infected herds can also influenced by size and other management practices (Ståhl et al., 2008; Brooks-Pollock and Keeling, 2009). Therefore, the absolute values predicted by the model should be interpreted with caution, but the general trends should be robust.

Conclusion

The study findings have important implications from both a financial and epidemiological perspective. Herds that are operating below industry targets for reproductive performance are not only undermining profitability at the farm level, but are also contributing to the persistence of many economically important pathogens at the industry level. The wide variation in reproductive performance between herds suggests that there is significant potential to reduce the number of replacement breeding cattle purchased and therefore the number of potentially infectious contacts by improving herd reproductive management. As a disease control strategy, this approach may be particularly effective because of its ability to target multiple pathogens simultaneously while having easily demonstrable effects on farm profit margins.

Chapter 7

Controlling endemic diseases through the targeted manipulation of network structure

Summary

Cattle movement networks have many characteristic structural features that drive the epidemiological behaviour of directly transmissible endemic diseases. The purpose of this analysis was to determine whether transmission dynamics could be altered by placing targeted constraints on contact formation to reconfigure movement network topology. This was accomplished with a simple network generation algorithm that used configuration wiring to preserve the empirical contact distribution and stochastic blockmodelling to change the probability of contact formation between farms based on specified demographic or network characteristics. The greatest reductions in endemic prevalence were observed for networks where highly connected farms were made to preferentially form contacts with other highly connected farms (assortative mixing) and for networks where the betweenness centrality of individual contacts was minimized. In both cases, the effect was most likely attributable to the significant increase in network fragmentation. Reducing the total number of contacts in the network by matching farms based on their absolute supply and demand for cattle had only modest effects on transmission dynamics, while introducing restrictions to make the network more spatially clustered made almost no detectable difference. Across all network generation algorithms, the relative magnitude of the predicted changes in endemic prevalence was greater for diseases with short farm infectious periods and low transmission probabilities. Poor correlation between individual network structural topology measures and endemic prevalence highlights the limitations in using standard network analysis tools to make inferences about disease behaviour on dynamic contact networks. Overall, the study findings demonstrate that substantial

epidemiological benefits can be gained through disease control measures aimed at generating movement networks with more favourable topological configurations.

Introduction

The British cattle population hosts a diverse community of endemic pathogens that undermine industry profitability through their collective impact on animal health and performance (Bennett et al., 1999a). As such, a tremendous amount of ongoing research is dedicated to finding more cost-effective means of preventing and controlling disease outbreaks in affected cattle herds. Given the challenges in developing robust epidemiological models, most studies to date have focused on single pathogens when evaluating the relative costs and benefits of different control interventions (Schepers and Dijkhuizen, 1991; Vonk Noordegraaf et al., 1998; Stott et al., 2005; Weldegebriel et al., 2009). However, none of these diseases exist in isolation and in a recent review, Carslake and colleagues (2011) emphasized the importance of targeting management practices that serve as common risk factors for multiple endemic diseases as a potential means of reducing trade-off in resource allocation.

Cattle movements have come under particular scrutiny over the past decade both because of their central role in the epidemiology of many economically important livestock pathogens (Van Wuijckhuise et al., 1998; Alban et al., 2001; Gilbert et al., 2005) and because the movements of individual cattle have been explicitly recorded in a computerized database since 1998 as part of the European Union's livestock traceability requirements (Mitchell et al., 2005). The latter has enabled researchers to construct highly detailed models of disease transmission dynamics at the population level (Kao et al., 2006; Green et al., 2008; Keeling et al., 2010; Tinsley et al., 2012). Similar to other biological and social systems, it has been shown that cattle movements organize into complex and dynamic contact networks with several key features relevant to infectious disease control (Martínez-López et al., 2009b). For example, the contact or degree distribution is often highly

right skewed, meaning that a small number farms have a disproportionately large number of contacts. This leads to the emergence of scale-free behaviour characterized by the absence of epidemic thresholds in large populations (Barabasi, 2009), higher basic reproduction numbers (R_0) than expected for networks with uniform degree distributions (Woolhouse et al., 2005), and greater tolerance to control measures applied at random (Albert et al., 2000).

In addition, cattle movement networks also display small-world properties characterized by the local clustering of contacts with the occasional long distance jumps that are responsible for spreading disease to more distant network communities (Watts and Strogatz, 1998). From an epidemiological perspective, removing the subset of high risk farms and high risk movements from the network has consistently been reported as the most cost-effective means of controlling disease at the population level (Natale et al., 2009; Natale et al., 2011; Rautureau et al., 2012). However, the recommended interventions, such as vaccinating herds to mitigate the risk of severe disease outbreaks or testing purchased cattle to prevent disease introductions, are often highly pathogen specific. Furthermore, many endemic diseases have a subclinical carrier state for which there are few reliable ante-mortem diagnostic tests and for which quarantine or treatment is unlikely to be effective (Lindberg and Alenius, 1999; de la Rua-Domenech et al., 2006; Nielsen and Toft, 2008). With the high rate of contact turnover in cattle movement networks (Vernon, 2011), it can also be difficult to predict in advance which movements are most likely to have a central role in spreading disease.

Numerous theoretical studies have shown that the transmission dynamics of many infectious pathogens can be changed by modifying specific structural properties of the contact network. For example, increasing network clustering almost invariably slows epidemic spread due to the rapid depletion of local susceptible contacts (Holme and Kim, 2002; Newman, 2003; Volz et al., 2011). In assortative networks where highly connected individuals form contacts with other highly connected individuals, disease tends to spread more rapidly (Newman, 2002;

Kiss et al., 2008), but the probability of extinction is greater (Nishiura et al., 2011) and fewer individuals become infected over the course of the epidemic (Badham and Stocker, 2010). Other researchers have also explored the effects of homogenizing the degree distribution (May and Lloyd, 2001; Pastor-Satorras and Vespignani, 2002; Ames et al., 2011) or introducing higher order community structures (Liu and Bambi, 2005; Salathé and Jones, 2010). Although the primary objective of these analyses has been to emphasize the importance of accounting for non-random behaviour in epidemiological models, the findings also highlight the potential for controlling many diseases simultaneously by manipulating contact patterns.

The concept of restricting animal movements to control disease is by no means new to veterinary epidemiology (Fèvre et al., 2006). In the United Kingdom, there has been long standing legislation that prevents farms with bovine tuberculosis from selling cattle until the herd is cleared from infection and more recent legislation that requires all cattle moved from endemic regions to be tested for bovine tuberculosis within 60 days prior to the movement. Movement standstill legislation has also been in place since 2001 to limit the potential undetected spread of foot-and-mouth disease through animal movements. As the result of farm behavioural adaptations, there have been unintentional changes to the contact network structure that may have positive (Gates et al., 2013), negative (Robinson et al., 2007), or mixed (Vernon and Keeling, 2012) effects on disease transmission dynamics. Little is currently known about the effects of intentionally manipulating contact patterns due to the lack of network generation models that are simple enough to be computationally tractable, yet complex enough to capture important epidemiological features of cattle trade behaviour.

In this analysis, a series of network generation algorithms were developed from first principles to determine whether the transmission dynamics of endemic cattle pathogens can be altered by changing movement network topology. These include algorithms designed to modify the degree distribution, assortativity, spatial clustering, and connectivity of the empirically observed British cattle movement

network from 2006. The results are used to highlight the complex relationship between network structure and disease behaviour as well as to identify potential opportunities for controlling multiple endemic diseases simultaneously through targeted movement restrictions.

Methods

Cattle movement data

Records of all cattle births, deaths, and movements in Great Britain are stored in the electronic Cattle Tracing System (CTS) database operated by the British Cattle Movement Service (BCMS). Data is provided to researchers as a series of tables that can be linked through the unique identification number of either the animal or the movement location. This analysis focused on movements between locations classified as agricultural holdings, landless keepers (farmers that raise cattle on rented land), and livestock markets during the period from 01 January 2006 to 31 December 2006. Movements to showgrounds and abattoirs were excluded from the analyses as they are believed to have a negligible role in the transmission of endemic cattle pathogens. Each movement record contained basic information on the animal identification number, departure location, destination location, and movement date. For movements that occurred through a livestock market, the on-movement record was paired with the corresponding off-movement record to preserve the identity of the source and destination herds. It was assumed that disease transmission between individual cattle at market was also negligible.

The network generation model was parameterized using data from 01 January 2006 through 31 December 2006. The primary justification for selecting this year was to ensure that sufficient pre- and post-movement data was available to determine the production purpose of each animal at the time of movement. It was assumed that animals intended for human consumption would be slaughtered by 30 months of age to comply with bovine spongiform encephalopathy (BSE) regulations

and at the time of the study, CTS data were only available through April 2010. Animals were classified into one of three production groups based on their breed, gender, age of death, and recorded calvings: beef breeding female, dairy breeding female, and store cattle (including male store cattle, female store cattle, and an unknown number of breeding bulls). The breeding female groups included animals with at least one recorded calving in the CTS database and animals that survived beyond 30 months of age.

All cattle farms in Great Britain are assigned a unique County-Parish-Holding (CPH) number in addition to their unique CTS location identifier, which allows them to be consistently georeferenced to the county and agricultural parish levels. A GIS map containing the agricultural parish boundaries was used to generate easting and northing coordinates for the parish centroids. Although the CTS database contains a data table listing farm addresses and ordinance survey coordinates, this information is available for only 68% of herds (Mitchell et al., 2005). Furthermore, the address listed in the CTS database may be for the main farm business and not the actual address of cattle premises. The Euclidean distance between parish centroids for the departure and destination farms was therefore used as an approximate estimate of movement distance.

The individual movement records were subsequently assembled into batch movement records such that all cattle of a single production type moved from one holding to another during a given calendar month were considered a single batch. Each batch movement record contained the following information: departure farm identification number, departure farm parish, destination farm identification number, destination farm parish, movement date, animal production type, market identification number (dummy coded 0 for movements that occurred directly from farm to farm), and movement distance. It was also recorded whether the movement was repeated during multiple months of the year and whether the movement had a reciprocal edge. The latter was defined as having both a directed movement from

farm A to farm B and a directed movement from farm B to farm A at any point during the calendar year.

Basic network generation model

The network generation model was based on the assumption that the number of inward and outward contacts made by each farm within a given calendar month was fixed. The objective was not to produce an exact replicate of the observed cattle movement network, but rather to provide a framework for comparing the relative effects of rewiring the movement network under different topological constraints. To preserve the contact distribution, a modified version of the configuration wiring algorithm (Serrano and Boguna, 2005) was used as follows:

1. Each farm in the population was assigned a fixed number of outward "stubs" and inward "stubs" corresponding to the observed out-degree and in-degree within the calendar month. The system was assumed to be closed so that the total number of outward stubs was always equal to the total number of inward stubs. Each stub was created as a virtual object with the basic attributes of farm identification number, month, and animal production type. At the beginning of each network wiring simulation, the lists of outward stubs and inward stubs were ordered randomly to prevent biases in contact selection.

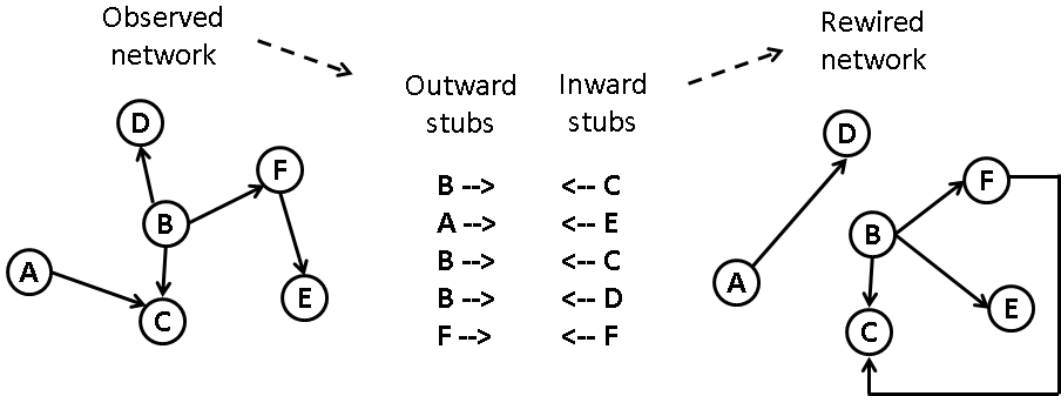
2. Working down the list of outward stubs, potential inward stub contacts were chosen at random and when a suitable match was found, the corresponding farms were connected by a directed edge. Stubs were only allowed to form connections if the inward stub occurred in the same month and had the same animal production type as the outward stub. No loop or multiple edges were allowed to form within in a given month and once a connection was made, the choice of contacts for the next outward

stub was inherently limited to remaining inward stubs. The process continued until all outward stubs were matched with an inward stub.

3. Each new movement edge was assigned a random date drawn from the empirical distribution of movement dates observed within the month. No attempts were made to model the fine scale temporal dynamics of cattle movements for individual farms such as the timing between on movements and subsequent off movements. These are important considerations for modelling the spread of fast moving epidemics like foot-and-mouth disease (Tildesley et al., 2011), but are less likely to impact the transmission dynamics of endemic diseases that spread over much longer time scales .

A schematic representation of the network generation algorithm is shown in Figure 7.1. The algorithm was developed in the C programming language and rigorously tested to ensure there were no coding errors. The output from each simulation was an edge set containing the departure farm identification number, destination farm identification number, and movement date. Since the degree distribution was preserved within each calendar month, the resulting edge sets always contained the same total number of batch movements for the entire calendar year.

Figure 7.1: Schematic representation of the basic network generation algorithm



Rewiring algorithms

The basic network generation algorithm was modified to create networks with the 12 different configurations described below. The method for introducing contact restrictions in the model was similar to the stochastic blockmodel described by Karrer and Newman (2011). In this system, individuals are assigned into one of *K* groups based on their specified demographic or network characteristics. The probability of individuals from any two groups forming a contact can be modified to produce networks with a wide variety of different structures. Here the algorithms either completely restricted contacts between groups or changed the preferential order in which contacts were allowed between individuals in different groups as appropriate.

Irrespective of the additional constraints introduced by each algorithm, outward stubs were only ever allowed to form contacts with inward stubs that had the same month and animal type attributes. The order of the outward stubs list was always randomized at the start of each simulation replicate to reduce potential bias in contact selection resulting from the order in which stubs were matched. It should be noted that the algorithms were designed to highlight general trends in the effects of network topology on disease transmission dynamics rather than to optimize the networks for the specified feature. This was due to the computational limitations of working with large contact networks. It was also impossible to change any single network property in isolation and the differences between the rewired networks are apparent in multiple network measures.

Observed network

As a baseline for comparison, these networks used the observed set of movement edges. However, the movement dates were selected at random based on the procedure described in step 3 of the basic network generation algorithm. The purpose for doing this was to make the temporal structure of the observed network as similar as possible to the temporal structure of the rewired networks. This

ensured that any of the observed differences in transmission dynamics could be attributed to the structural changes in the network rather than the inability of the rewiring algorithms to capture fine scale temporal patterns in the sequence of on and off movements to the farm.

Market utilization

These two algorithms were designed to explore the effects of market selection and utilization on network mixing patterns. In the first algorithm (market), outward stubs were only allowed to form connections with inward stubs that had the same livestock market attribute. Movements that occurred directly from farm to farm were grouped together in a single market category. The second algorithm (random) represented the least constrained model in which outward stubs were allowed to form connections with any other inward stub in the network at random.

Assortative mixing

These algorithms were designed to generate networks with high assortativity (assortative) and low assortativity (disassortative). Farms were ranked according to the total number of connections made during the calendar year and split into decile groups. Each stub was then assigned the attribute of farm degree decile. In step 1 of the network generation algorithm, the outward stub list was ordered by decile from top to bottom and then randomly within each decile. In step 2, outward stubs were made to preferentially attach to inward stubs within the same decile group. If an appropriate match could not be found within the same decile group, the outward stubs were allowed to make connections with inward stubs in the next lowest decile group. The disassortative algorithm operated similarly except that outwards stubs in the highest decile groups were preferentially made to form contacts with inward stubs in the lowest possible decile group.

Degree distribution

These algorithms were designed to generate networks with the fewest number of contacts (fewest contacts) and greatest number of contacts (most

contacts) by matching farms based on their absolute supply and demand for cattle. To minimize the number of contacts, each farm was assigned a single stub for each production type of animal purchased or sold within each month. The stub was assigned the attribute of total number of cattle. The system was again assumed to be closed so the total number of cattle sold was always equal to the total number of cattle purchased. In step 2 of the network generation algorithm, farms were preferentially made to form attachments with farms that purchased the same number of cattle. If an identical match could not be found, farms were allowed to form contacts with the next closest match. The number attribute of each stub was updated accordingly and the process was repeated until all cattle for the stub were matched. To maximize the number of contacts, each farm was assigned a number of stubs equal to the total number of cattle bought or sold. Contacts were then made at random using the network generation model as originally described. In these networks, the maximum number of contacts was almost always equal to the total number of cattle bought or sold.

Spatial clustering

These algorithms were designed to explore the effects of making the networks more spatially clustered by having outward stubs preferentially form attachments to inward stubs in the same or next closest geographical unit. The geographical units tested were network trade community (community), administrative county (county), and agricultural parish (parish). The network trade communities were identified using the walktrap community detection algorithm proposed by Pons (Pons and Latapy, 2005). Briefly, this algorithm assumes that short random walks performed on the network are more likely to stay within the same community due to their higher density of connections. To reduce the computational time, the agricultural parishes were used as nodes and the weighted movements between them were used as edges. A total of 8 major trade communities were identified, which included 9,257 of the 12,497 agricultural parishes in Great

Britain. The remaining parishes either had no farm to farm cattle movements or were assigned to disconnected communities with fewer than 10 agricultural parishes

The geographic boundaries of the trade communities were smoothed by aggregating the parish membership at the county level and each farm was accordingly assigned the attribute of community. The attributes of county and parish were obtained directly from the farm CPH code. For step 2 of the network generation algorithm, a Euclidean distance matrix was generated between all pairs of geographical units. Outward stubs were made to preferentially form attachments with inward stubs in the same geographical unit and if an appropriate match could not be found, the next closest unit was searched for a match and the process repeated until all stubs were matched.

Betweenness centrality

These algorithms were designed to promote the formation of contacts with low predicted betweenness centrality (lowest betweenness) or high predicted betweenness centrality (highest betweenness). Simple disease simulations were first performed to confirm the importance of edge betweenness centrality to network transmission dynamics. The observed network edges were first ranked according to their betweenness centrality score. At the start of each simulation, a random proportion of edges between 0 and 0.5 were removed in order of betweenness centrality. Using the disease simulation model described in Section 2.4, the resulting endemic prevalence was estimated for a disease with an average farm infectious period of 1095 days and a transmission probability of 0.05 similar to bovine viral diarrhoea virus (Tinsley et al., 2012). A total of 10,000 replicates were performed. As a baseline for comparison, a second set of simulations was performed where the edges were removed arbitrarily. These results confirmed that the top 10% of edges with the highest betweenness centrality scores had a disproportionately strong influence on transmission dynamics.

The next step was to generate a multivariate logistic regression model to predict the probability that an edge would have a high betweenness centrality score

based on the demographic characteristics of the source and destination herd. The sample included all unique edges from the empirically observed data set and a case was defined as edge that ranked in the top 10% for betweenness centrality. The independent variables in the model included (1) departure herd type, (2) departure herd size, (3) departure herd in-degree, (4) destination herd type, (5) destination herd size, (6) destination herd out-degree, (7) movement distance, and binary variables to describe whether the movement was (8) inter-community, (9) inter-county, (10) inter-parish, (11) reciprocal (defined as a bidirectional edge), or (12) repeated within the year. Herd size was estimated as the average number of cattle present on given day during the calendar year. The herd type variable had four levels: other, beef breeding herd, dairy breeding herd, or mixed breeding herd based on the presence of recorded calvings by dam breed classification in 2006. The continuous variables were log transformed prior to analysis due to their highly right skewed distributions.

All variables were found to be significant in both the univariate and multivariate models at the $p < 0.001$ level. The equation from the final multivariate logistic regression model was retained for use in the network generation algorithm. In step 1 of the algorithm, the outward stub list was first ordered by degree decile and then randomly within each decile group. Then for each outward stub, the list of all remaining inward stubs was searched to find the connection with the lowest predicted probability of forming an edge with high betweenness centrality based on the movement characteristics. The same methodology was used to generate networks with high betweenness centrality edges, except the list of inward stubs was searched to find the connection with the greatest probability of having a high betweenness centrality score.

Network characterizations

The effects of altering movement network topology were assessed using both standard network topology measures and simple dynamic disease simulation models. The network topology measures included assortativity, average path length, median

edge betweenness centrality, clustering coefficient, density, degree, diameter, median Euclidean distance, fragmentation index, and the size of the giant strongly connected component (GSCC). Definitions of these measures are provided in Figure 7.1 along with brief descriptions of their proposed epidemiological significance. The mean and standard deviation of the values for 50 network replicates were calculated using the igraph library for in the C programming environment (Csardi and Nepusz, 2006).

The disease transmission model was based on simple susceptible-infectious-susceptible (SIS) dynamics. At the beginning of each simulation, disease was seeded on 10% of farms at random on 01 January 2006. Each affected farm was assigned an infectious period drawn at random from an exponential distribution with a half-life of *h* days. The model was then updated in time steps of one day. If an infected farm moved a batch of cattle to a susceptible farm, there was a fixed probability, *p*, that the destination farm would also become infected. Farms that reached the end of their infectious period reverted back to a susceptible state. To ensure adequate time for the system to reach steady state equilibrium, the simulation was allowed to run for a total of 25 years by recycling the single year of movement data from the rewired network. Endemic prevalence was measured as the average number of farms infected on any given day over the last 3 years of the simulation. The simulation code was implemented in the C programming language. A total of 9 disease parameter combinations were tested for each of the 12 network generation algorithms using the infectious periods of 365 days, 1095 days, and 1825 days and the transmission probabilities 0.05, 0.15, and 0.25. The purpose was to determine whether the effects of network rewiring varied based on the pathogen characteristics. A total of 250 simulations were run for each parameter combination with a uniquely rewired network used at the beginning of each simulation. This number was selected by running performance curves for each network generation model. The average endemic prevalence for each parameter combination and each network generation algorithm was calculated.

Table 7.1: Definition and proposed epidemiological significance of summary statistics used to characterize structural features of cattle movement networks.

Network Measurement	Definition
Assortativity	The tendency for farms to make contacts with other farms of similar degree. Negative values indicate disassortative networks where high degree farms make more frequent contact with low degree farms. Positive values indicate assortative networks, meaning that high degree farms make more frequent contact with other high degree farms. Epidemics on assortative networks tend to have faster initial growth rates and shorter durations (Kiss et al., 2008).
Average path length	The average distance required to reach any given farm from any other farm in the network along a series of shortest paths (Watts and Strogatz, 1998). Average path length is positively correlated with the time taken to reach maximum epidemic size (Shirley and Rushton, 2005). The 'closer' farms are in network distance, the faster disease can spread.
Betweenness centrality	The number of shortest paths between two farms in the network that pass through a particular farm. Farms with high betweenness centrality contribute disproportionate amount to transmission events and may be responsible for bridging distant communities in the network.
Clustering coefficient	The probability that any two immediate neighbours of a farm are also directly connected. When disease is introduced to a highly clustered network, it tends to rapidly saturate local susceptible contacts and maximum epidemic size is reduced unless there are many links bridging local clusters (Keeling, 1999; Newman, 2003).
Degree	The number of incoming or outgoing connections associated with each node. In simulation models, epidemics seeded on farms with high degree spread faster and infect more farms than epidemics seeded on farms with few contacts (Moslonka-Lefebvre et al., 2009; Pautasso et al., 2010).
Density	The proportion of all possible connections between nodes that are observed in the network.
Diameter	The length of the longest path between farms in the network.
Fragmentation index	The proportion of pairs of farms that are not connected by any path.
Giant strongly connected component (GSCC)	The largest subset of farms that are mutually reachable via directed links. For every pair of farms *i* and *j* in the GSCC, if there is directed path from *i* to *j*, there implicitly must also be a directed path from *j* to *i*. By definition, an epidemic seeded in GSCC has the potential of spreading to all other farm in the GSCC and has therefore been widely used to estimate the lower bounds of an epidemic (Kenah and Robins, 2007b, a).

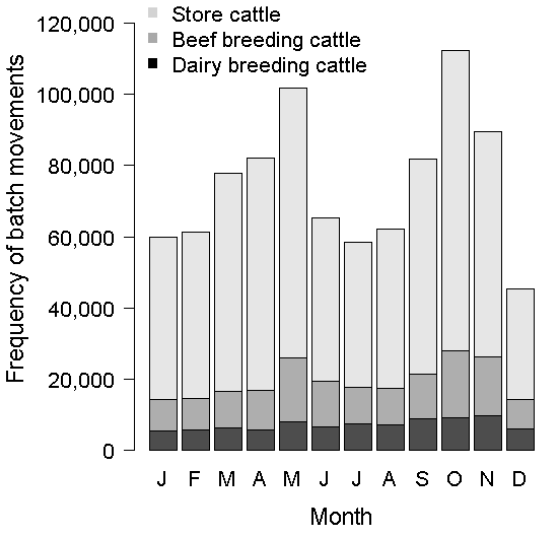
The relationship between individual network structural topology measures and endemic prevalence for a disease with an average infectious period of 1095 days and a transmission probability of 0.05 was assessed using the Pearson product-moment correlation (r). The results were expressed as the coefficient of determination (r^2) and the significance level was set at $p < 0.05$. Correlations between network structural topology measures were also explored.

Results

Descriptive statistics

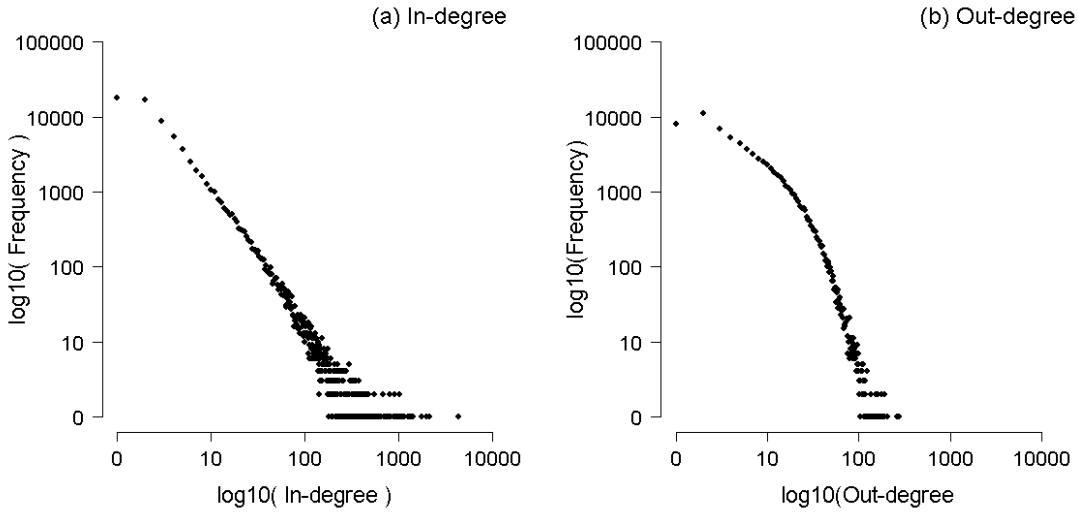
The observed cattle movement network contained 889,320 batch movements between 74,444 cattle farms. Due to repetition in movements between months and animal production types, there were only 682,510 unique edges in the resulting network. As shown in Figure 7.2, the majority of batch movements (74.1%) were attributable to animals classified as store cattle, while the movements of beef and dairy breeding cattle accounted for 16.3% and 9.6% of all batch movements, respectively. Seasonal peaks in cattle movements were observed in late spring and autumn.

Figure 7.2: Frequency of batch movements by month and animal production type.



The in-degree and out-degree distributions were both highly right skewed with the majority of farms making relatively few contacts over the course of a year (Figure 7.3). Although there was a significant correlation between the in-degree and out-degree, the strength of the association was weak ($r = 0.12$, $p < 0.001$).

Figure 7.3: Log-log plots of the (a) in-degree distribution and (b) out-degree distribution.

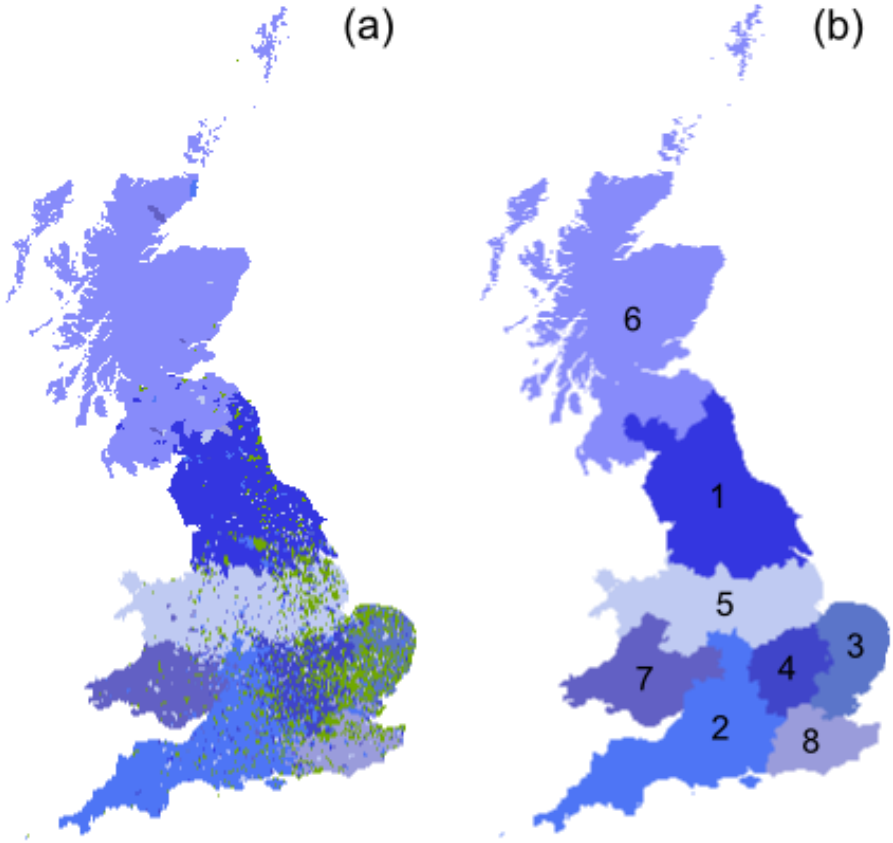


Movements through the 141 recorded auction markets accounted for 72.6% of all batch movements, but only 53.7% of the total number of cattle moved. On any given market day, farms that sold cattle made contact with an average of 2.36 farms (median: 2, range: 1 to 88), while farms that purchased cattle made contact with an average of 3.11 farms (median: 2, range: 1 to 88). The median distance of direct farm to farm movements was 18.4 km compared to 51.8 km for movements that occurred indirectly through auction markets.

The walktrap community detection algorithm identified 8 major trade communities, which included 75% of all agricultural parishes in Great Britain. Although the agricultural parishes within each community were generally spatially clustered, the boundaries were not always distinct (Figure 7.4). A particularly high

number of agricultural parishes in the southern and eastern parts of England either had no cattle movements or were disconnected from the network.

Figure 7.4: Membership of (a) agricultural parishes and (b) counties in the trade communities identified through the walktrap community detection algorithm. Parishes highlighted in green either had no farm to farm cattle movements or belonged to communities with fewer than 10 parishes.



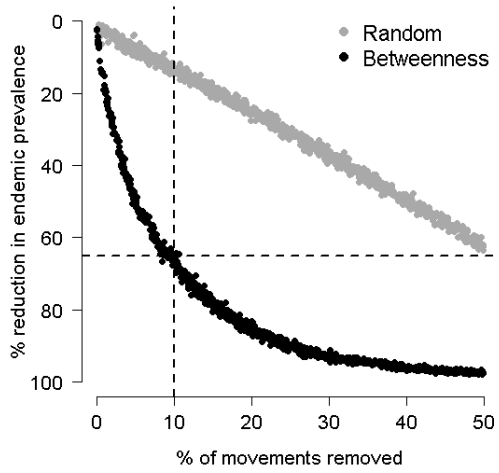
After reassigning farms into the communities outlined in Figure 7.4b, the total number of movements within and between individual communities were tabulated (Table 7.2). With the exception of Scotland (community 6), the majority of communities were either significant net importers or significant net exporters of cattle.

Table 7.2: Total number of individual cattle movements ($x10^3$) within and between trade communities.

	1	2	3	4	5	6	7	8	Total	Net cattle
1	482.7	2.9	2.4	1.0	25.9	37.0	1.4	0.5	**553.8**	**72.7**
2	29.8	503.0	19.7	23.8	28.9	2.0	13.1	9.2	**629.6**	**-75.1**
3	1.3	1.2	38.6	3.5	3.8	0.3	0.2	0.9	**49.6**	**29.3**
4	0.9	9.2	3.9	34.4	6.9	0.2	1.0	1.1	**57.5**	**26.5**
5	52.1	9.1	5.2	9.4	368.4	5.2	19.7	0.2	**469.2**	**15.6**
6	42.8	0.7	0.2	0.1	2.0	409.8	0.3	0.1	**456.0**	**0.2**
7	16.5	22.1	1.6	5.1	47.4	1.4	201.9	0.4	**296.3**	**-58.1**
8	0.5	6.5	7.5	6.6	1.6	0.3	0.6	43.5	**67.0**	**-11.1**
Total	**626.5**	**554.5**	**79.0**	**84.0**	**484.8**	**456.1**	**238.1**	**55.9**	**2579.0**	**0.0**

Edges with a high betweenness centrality had a disproportionately strong influence on disease transmission dynamics. For an endemic disease with an average infectious period of 1095 days and transmission probability of 0.05, removing movements ranked in the top 10% for betweenness centrality reduced the endemic prevalence by 65% (Figure 7.5). In contrast, removing 10% of movements at random reduced the endemic prevalence by only 13.5% on average.

Figure 7.5: Estimated reduction in endemic prevalence following the removal of edges at random or ranked by betweenness centrality. The dashed lines highlight the effects of removing the top 10% of edges ranked by betweenness centrality.



All variables included in the multivariate logistic regression model were significant predictors of high edge betweenness centrality (Table 7.3). The odds of a movement having a high betweenness centrality increased with the in-degree of the departure herd, the out-degree of the destination herd, and when the movement was between trade communities or had a reciprocal edge. Departure herd size, destination herd size, movement distance, and being a repeated edge were protective factors. Movements between farms in different counties and between farms in different parishes also had significantly decreased odds of being high betweenness centrality edges than movements within the same geographic unit. Movements originating from breeding herds had decreased odds of being high betweenness centrality edges, while those terminating in breeding herds were at significantly increased risk.

Table 7.3: Results from the multivariate logistic regression model of risk factors for high edge betweenness centrality.

Variable	Level	Coeff	OR	95% CI	p-value
Intercept	-	-1.343	-	-	-
Departure herd					
Type	Beef	-0.102	0.90	0.88 – 0.93	< 0.001
	Dairy	-0.490	0.61	0.59 – 0.64	< 0.001
	Mixed	-0.302	0.74	0.71 – 0.77	< 0.001
Size	$\log_{10}$	-0.501	0.61	0.59 – 0.62	< 0.001
In-degree	$\log_{10}$	1.720	5.59	5.49 – 5.68	< 0.001
Destination herd					
Type	Beef	0.979	2.66	2.60 – 2.73	< 0.001
	Dairy	1.741	5.71	5.50 – 5.92	< 0.001
	Mixed	1.197	3.31	3.21 – 3.41	< 0.001
Size	$\log_{10}$	-1.100	0.33	0.33 – 0.34	< 0.001
Out-degree	$\log_{10}$	1.159	3.19	3.13 – 3.25	< 0.001
Distance (km)	$\log_{10}$	-0.182	0.83	0.81 – 0.86	< 0.001
Edge type					
Intercommunity	Yes	0.363	1.44	1.41 – 1.47	< 0.001
Intercounty	Yes	-0.096	0.91	0.89 – 0.93	< 0.001
Interparish	Yes	-0.399	0.68	0.63 – 0.71	< 0.001
Reciprocal	Yes	0.823	2.27	2.20 – 2.36	< 0.001
Repeated	Yes	-1.359	0.26	0.25 – 0.27	< 0.001

Network structural topology

The effects of imposing rewiring constraints on various measures of network structural topology are shown in Table 7.4. Networks that were rewired to increase assortativity had significantly higher fragmentation indices, longer diameters, and smaller GSCC sizes compared to randomly rewired networks. However, there was little difference in the average path length, degree, and network density. The structural features of disassortative networks were similar to those of randomly rewired networks with the exception of slight decrease in the network diameter and fragmentation index and a slight increase in the average path length and GSCC size.

By matching farms based on their supply and demand for cattle in a given month, it was possible to reduce the total number of batch movements in the network by 31.5%. This reduced the average degree from 11.88 to 8.27 and increased the average path length from 4.84 to 5.64, but otherwise had little appreciable effect on network topology. In the worst case scenario where each individual animal that was bought or sold created a unique contact, the total number of batch movements was increased by 290%. This increased the average degree to 34.2, while reducing the average path length to 3.56 and the diameter to 11.86. The assortativity, fragmentation index, and GSCC size were largely unchanged.

Imposing spatial restrictions on the process of contact formation significantly reduced the average movement distances. The mean distance for randomly rewired networks was 285 km (median: 250 km), compared to 120 km (median: 99) in networks rewired by community, 69 km (median: 46 km) in networks rewired by county, and 53 km (median: 18) in networks rewired by parish. In the observed 2006 movement network, 81.5% of movements took place between farms in the same community.

In contrast, intra-community trade was responsible for 18.4% of movements in the randomly rewired networks, 91.4% in the networks rewired by community, 54.2% in the networks rewired by county, and 82.5% in the networks rewired by parish. Approximately 86.0% of the inter-community movements in the networks

rewired by community were to and from farms located in southern Wales. As the network rewiring became more spatially restricted, the average path length, clustering coefficient, diameter, and GSCC size increased, while the degree, density, and fragmentation index decreased. There were no obvious trends with assortativity.

Using the multivariate logistic regression equation in the network generation algorithm, it was possible to reduce the median edge betweenness centrality to approximately 136 compared to 2,549 in the observed network and 5,370 in the high betweenness network. This resulted in substantial increase in the average path length, network diameter, and fragmentation index. The size of the GSCC was reduced by approximately half.

Network transmission dynamics

As shown in Figure 7.6, networks rewired with the assortative and low betweenness centrality algorithms had the lowest predicted endemic prevalence across almost all disease parameter combinations. Compared to the observed network, the endemic prevalence was reduced by an average of 50.2% (range: 32% to 75%) for the assortative algorithm and 69% (range: 36% to 100%) for the lowest betweenness centrality algorithm. Allowing contacts to form at random, reducing the total number of network contacts, increasing the spatial clustering of network contacts all had minimal effects on endemic prevalence. Results from the disassortative, highest betweenness centrality, and most contacts algorithms provide general estimates of the upper theoretical bounds of disease transmission on the cattle movement networks. Across all network generation algorithms, the relative magnitude of the effects on endemic prevalence decreased as both the infectious period and transmission probability of the pathogen increased.

Table 7.4: Structural topology of cattle movement networks rewired under different contact constraints. For each algorithm, the mean value from 50 simulations is shown.

	Observed	Random	Assortative	Disassortative	Fewest contacts	Most contacts
Assortativity	- 0.077	- 0.066	- 0.039	- 0.102	- 0.086	- 0.079
Average path length	6.38	4.84	4.83	4.95	5.64	3.56
Median betweenness centrality	2,549	2,984	458	4,121	6,959	735
Clustering coefficient	0.014	0.004	0.012	0.001	0.002	0.017
Degree	9.16	11.88	11.80	11.89	8.27	34.2
Density ($x10^{-4}$)	1.23	1.59	1.58	1.60	1.11	4.86
Diameter	22.00	15.48	31.68	14.28	16.78	11.86
Median distance (km)	42.4	245	243	245	246	254
Fragmentation index	0.698	0.651	0.993	0.621	0.664	0.625
GSCC	40,877	43,965	6,008	45,807	43,167	45,602

Table 7.4 (continued)

	Lowest betweenness	Highest betweenness	Market	Community	County	Parish
Assortativity	- 0.089	- 0.086	- 0.073	- 0.078	- 0.093	- 0.092
Average path length	12.32	5.51	4.93	5.85	7.96	9.86
Median betweenness centrality	136	5,370	3,445	1,646	1,071	1,018
Clustering coefficient	0.001	0.001	0.012	0.014	0.033	0.038
Degree	9.11	8.76	11.23	11.65	11.01	8.96
Density ($x10^{-4}$)	1.22	1.18	1.51	1.56	1.48	1.20
Diameter	45.06	14.42	15.66	18.76	25.60	40.16
Median distance (km)	149	104	78	98	45	17
Fragmentation index	0.925	0.610	0.648	0.824	0.762	0.668
GSCC	20,347	46,470	44,187	25,729	36,176	42,837

Relationship between topology and transmission dynamics

The average path length, degree, diameter, fragmentation index, and GSCC were all significantly correlated with endemic prevalence across the different networks (Figure 7.7). However, the correlations were only moderate and there were outliers for each network measure that may have influenced the results. In combination, the average network degree and fragmentation index explained 88.6% of the total variation in endemic prevalence. There was no significant relationship between endemic prevalence and either the clustering coefficient or network assortativity. Amongst the network structural features, there was a strong negative correlation between the fragmentation index and the GSCC ($r = -0.99$, $p < 0.001$), while the average path length was strongly positively correlated with the diameter ($r = 0.88$, $p < 0.001$). Diameter was also moderately correlated with the fragmentation index ($r = 0.66$, $p = 0.019$). The trends were similar across all infectious period and transmission probability combinations, although the results are not shown.

Figure 7.6: Impact of network rewiring on the predicted prevalence of disease at equilibrium. The values for the observed network are the average proportion of farms infected at equilibrium. The values for the remaining network show the factor change in prevalence relative to the observed network.

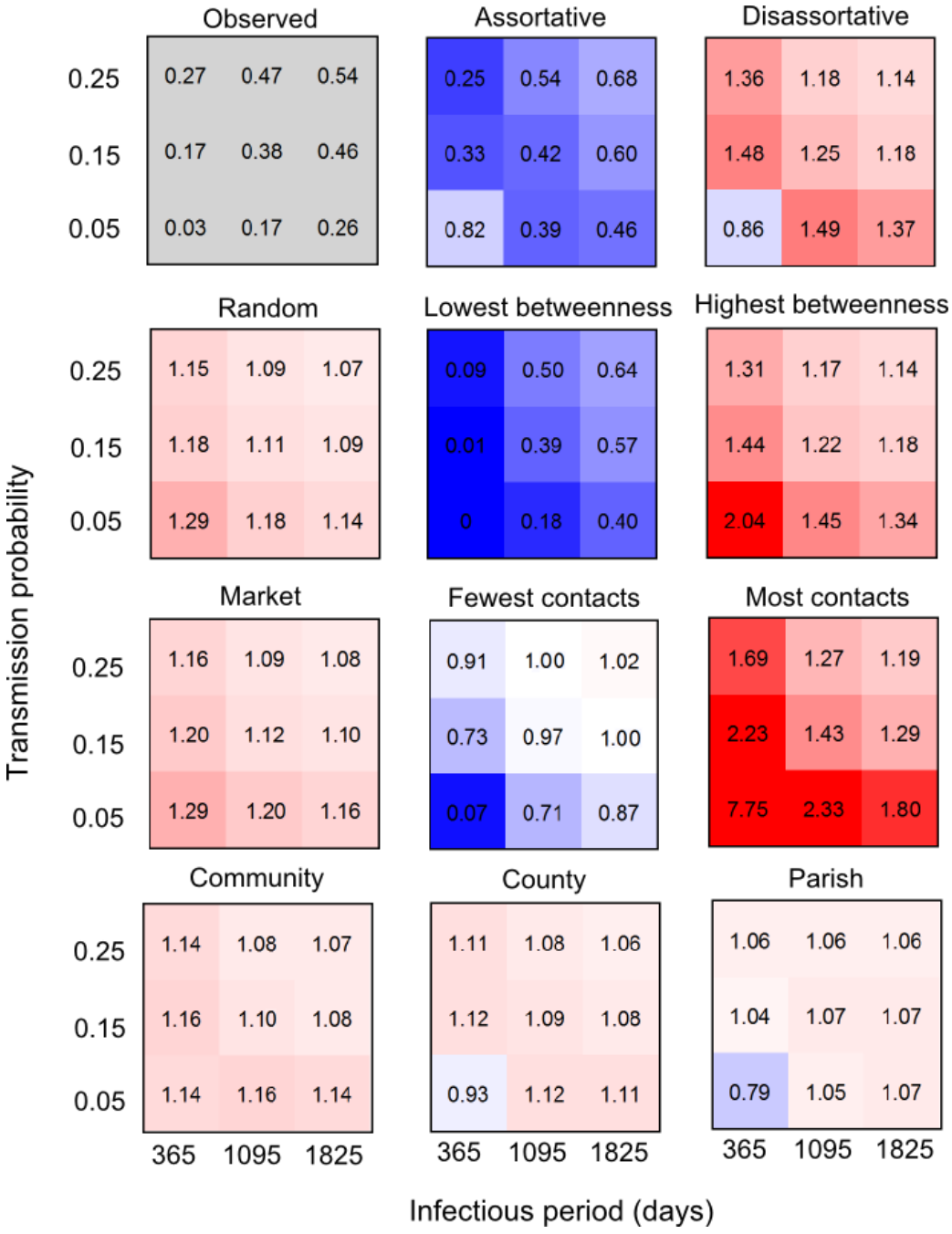
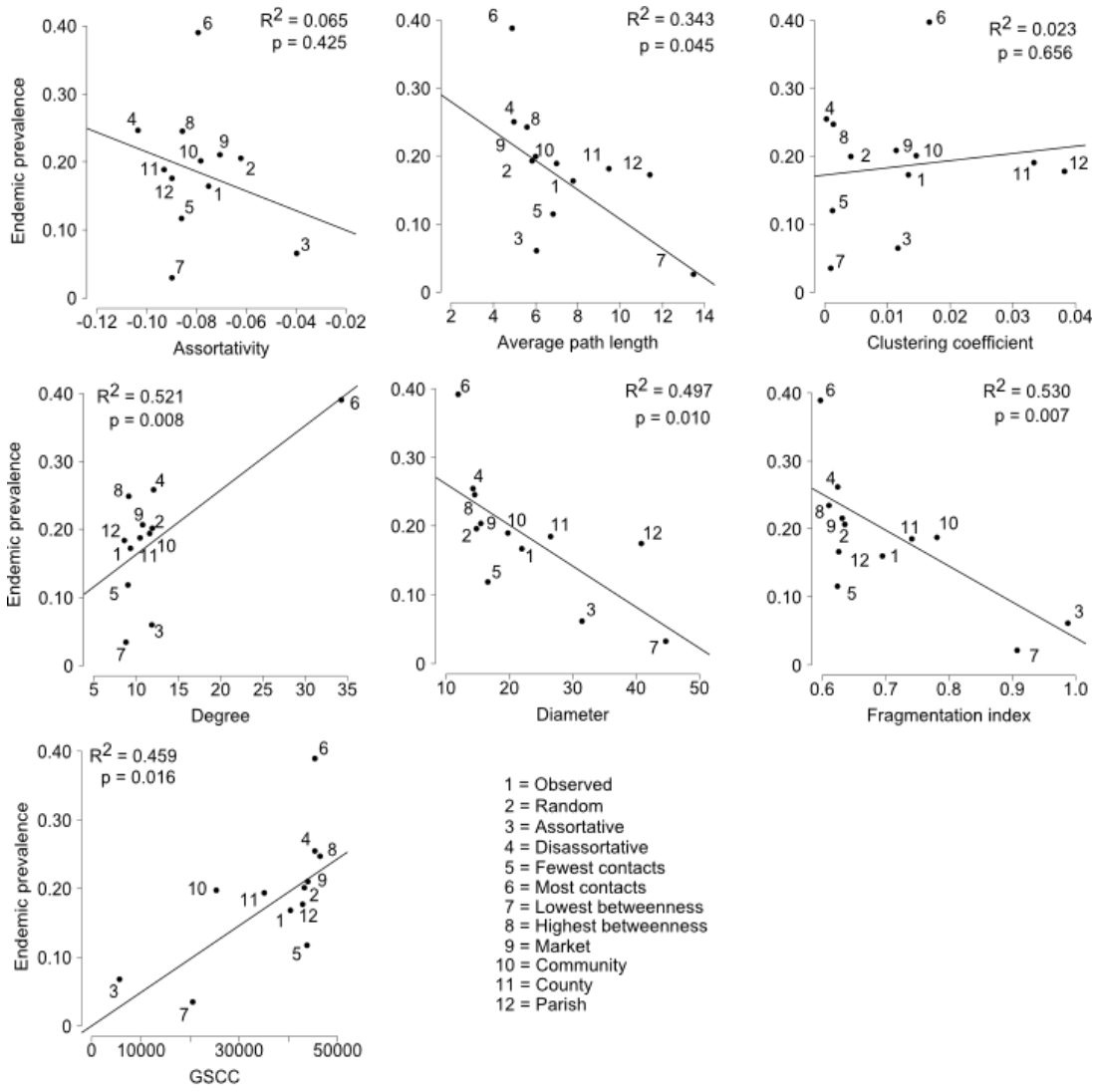


Figure 7.7: Correlation between network structural topology and predicted endemic prevalence for a pathogen with an infectious period of 1095 days and transmission probability of 0.05. The least squares regression line is shown.



Discussion

The study findings demonstrate that the transmission dynamics of endemic cattle pathogens can be substantially altered through movement restrictions that promote assortative mixing or prevent the formation of contacts with a high

predicted betweenness centrality. In both cases, the effects are most likely attributable to the significant increase in network fragmentation. For the assortative networks, the fragmentation stems from an increase in the number of dead end connections between farms, whereas the fragmentation in low betweenness centrality networks stems from an increase in network compartmentalization. Interestingly, the cattle movement network was highly resistant to changes in network assortativity. The maximum and minimum values from the algorithms were -0.039 and -0.102, respectively, which suggests that this property is constrained by the scale-free degree distribution.

As with many other livestock trade networks, physically removing the small number of batch movements with the highest betweenness centrality caused a disproportionately large reduction in endemic prevalence (Kiss et al., 2006; Green et al., 2009; Rautureau et al., 2010). Results from the multivariate logistic regression model suggest that movements into cattle breeding herds, movements to and from holdings acting as livestock dealers (low average herd size, high in-degree, and high out-degree), reciprocal movements, and movements between trade communities were at a particularly increased risk of have high edge betweenness centrality scores. Even if these movements cannot be prevented through targeted trade restrictions, it may possible to apply disease specific biosecurity measures such as quarantine, vaccination, or diagnostic testing to effectively remove them from the contact network.

The negative findings from the study provide just as important information about disease dynamics and control on cattle movement networks. It has previously been suggested that the closure of auction markets may increase the percolation of epidemic diseases by increasing the distances over which animals are animals are moved (Robinson and Christley, 2007). In the most unconstrained model where farms were allowed to form contacts at random, the median movement distances were almost 6 times greater than the observed network yet the predicted endemic prevalences were only 1.14 times greater on average. In the most spatially clustered

networks, the median movement distances were approximately 3 times less and there was still no appreciable change in transmission dynamics. This would suggest that structural topology of movement networks is largely independent of the spatial topology. However, it is possible that the effects of spatial clustering may be more protective for diseases such as bovine tuberculosis (Green et al., 2008) or bovine viral diarrhoea virus (Ersbøll et al., 2010) that spread through local transmission mechanisms in addition to cattle movements. Spatial clustering may also limit the rate and extent of transmission for diseases that are more geographically confined (Livingstone et al., 2006; Scott et al., 2006). In the simulation model, disease was seeded at random across the entire population of farms to mimic widespread endemic pathogens so these effects were not evaluated.

Under the assumptions of the network generation algorithms, it was also impossible to prevent the formation of intercommunity contacts. This was partly because the geographic boundaries used to define the communities were artificial and subsequently most communities became either net importers or net exporters of cattle. From a computational standpoint, there are few algorithms that can reliably detect community structure in large directed networks (Newman and Girvan, 2004) and even less empirical farm-level disease data to validate model predictions. In this analysis, the walktrap community detection algorithm was used due to its computational efficiency. However, others based on modularity, edge betweenness centrality, or eigenvectors may provide better approximations (Newman, 2004b, 2006). Even when communities are detected, the boundaries frequently overlap the administrative and political boundaries that are commonly used to allocate disease control resources (Lentz et al., 2010; Grisi-Filho et al., 2013). From a practical standpoint, the control measures used to isolate trade communities into epidemiological units must also be chosen carefully. Restricting intercommunity trade may have a significant impact on farming demographics if the supply and demand for cattle cannot be met through intracommunity trade.

Similar to Robinson and Christley (2007), descriptive statistics revealed that animals were most often bought and sold in small batches at market, which meant that cattle originating from a single farm were often distributed to multiple holdings and farms that purchased cattle often sourced cattle from multiple holdings. By matching farms based on their absolute supply and demand for cattle in a given month, it was possible to reduce the mean degree of cattle movement networks by up to 30%. However, the effects on endemic prevalence varied quite substantially based on the pathogen characteristics. For almost every network generation algorithm, the relative change in endemic prevalence compared to the observed network decreased as both the farm infectious period and transmission probability were increased. There was also less stochasticity in model predictions at higher parameter values. This suggests that diseases with a low basic reproduction number (R_0) are highly sensitive to changes in network topology. Other researchers have shown that the structural and temporal features of cattle movement networks matter less for diseases that spread over long time periods (Kao et al., 2007) or have a higher probability of spreading through batch movements (Vernon and Keeling, 2009).

In generating networks with different structural topologies, it was also possible to explore the complex relationship between static and dynamic network properties. Static network measures are often widely reported in the literature because they can be calculated with relative ease. However, they ignore many important epidemiological features of cattle movement networks such as the timing of movements on and off farms, the probability of disease spreading through a movement based on the number or production type of animals moved, and the within herd transmission dynamics that determine the farm infectious period. With the simple SIS model, it was only possible to assess the effects of movement timing and, similar to other theoretical studies, it was shown that single network measures were inadequate to describe transmission dynamics (Boily et al., 2007; Ames et al., 2011). For example, although the average size of the GSCC in networks rewired

with the community algorithm was approximately half that of the observed movement network, the endemic prevalence was actually predicted to be higher. The average path length also varied quite substantially between the spatial clustering algorithms and yet there was very little difference in the predicted endemic prevalence. This highlights the dangers in using changes in network structure to make inferences about changes in risk as previous research studies have done (Robinson et al., 2007; Bajardi et al., 2011; Mweu et al., 2013).

Although the model for generating contact networks was relatively simple, it offers many advantages over the traditional 'top down' algorithms that rely on arbitrary rules and scaling constants to replicate features from the observed contact network (Hakansson et al., 2010). The entire approach of generating contact from first principle is rapidly gaining traction in the social network field because of the need for accurate representations of human contact patterns to parameterize disease transmission models (Mahmood et al., 2010; Simini et al., 2012). Using the configuration wiring model, it was possible to capture both the empirical degree distribution as well as the directed nature of movement contacts. Introducing additional constraints through stochastic blockmodelling also allowed temporal and hierarchical structure to be incorporated in the models. The latter technique was used to generate contact networks with spatial clustering to study the transmission dynamics of the 2007 equine influenza outbreak in Australia (Firestone et al., 2011). To my knowledge, the only other published model of contact formation in livestock networks was proposed by Lindström and colleagues (Lindström et al., 2010; Lindström et al., 2013) and uses a Bayesian distance kernel to replicate spatial patterns in animal movements. To account for differences in animal production types, separate kernels were generated for beef and dairy farms.

For the model to be of use in guiding future policy decisions, there are several additional layers of complexity that must be considered. First, although contact formation was restricted by month and basic animal production type, farmers also choose to purchase cattle based on their specific breed, age, physical condition,

and reproductive status. This inherently reduces the number of potential network contacts, which would likely result in decreased the heterogeneity within and between network generation algorithms. Second, many contacts in the observed network were repeated multiple times during the year and also had reciprocal edges. These were most likely movements to and from seasonal grazing pastures or movements between uniquely identified land parcels owned by the same livestock business. It was not possible to confirm this with the available CTS data, but should be incorporated into future models. Third, by recycling the single year of rewired movement data in the disease simulation model, it was assumed that the number of contacts made by individual farms and the contact patterns remained fixed over time. However, both can change quite substantially from year to year, which may provide new transmission pathways that allow disease to spread more efficiently between herds (Volkova et al., 2010; Vernon, 2011). Finally, any restrictions to cattle movements are likely to impact industry profitability, especially if farmers must invest more time or travel further distances to trade their cattle. Thus the financial benefits of cattle movements must be carefully weighed against the epidemiological costs.

Conclusion

There is significant potential to reduce the prevalence of endemic cattle diseases by changing the structure of movement networks. From an epidemiological perspective, the most effective control strategies are those that increase network fragmentation by encouraging assortative mixing or preventing the formation of contacts with a high predicted betweenness centrality. However, there is a need for more sophisticated models to determine whether the financial benefits of controlling disease can justify the costs of restricting cattle trade.

Chapter 8

Quantifying the risks of bovine viral diarrhoea virus transmission through cattle movement networks

Summary

Network analysis has become a popular framework for studying how infectious diseases spread between herds through cattle movements. Traditionally, most models have assumed that all purchased cattle carry the same risk of generating outbreaks in the destination herd. Using data on bovine viral diarrhoea virus (BVDV) in Scotland as a case study, this analysis provides empirical and theoretical evidence that the risk of disease transmission varies substantially based on the animal and herd demographic characteristics at the time of purchase. The movements of replacement breeding cattle were responsible for only 12.1% of all individual cattle movements yet their targeted removal from the network resulted in a 2 times greater reduction in endemic prevalence than removing an equivalent number of movements at random. In particular, beef suckler herds that purchased pregnant heifers or open cows with a calf at foot and dairy herds that purchased open heifers were at increased risk of being seropositive for BVDV compared to other open herds. There was a significant non-linear relationship between herd size and seropositivity for beef suckler herds, which suggests that on-farm management factors such as the increased likelihood of implementing biosecurity measures or maintaining animals in separate production groups may protect larger herds against BVDV. Contrary to simulation model predictions, herd size had no significant effect on seropositivity in dairy herds, which suggests that recent cattle movements are weak predictors of herd serological status. These findings emphasize the importance of accounting for heterogeneity in animal production type and within-herd

demographic structure when modelling the network transmission dynamics of endemic cattle pathogens.

Introduction

Endemic diseases cause significant financial losses for the British cattle industry through their effects on animal health and performance (Bennett et al., 1999a). As such, researchers are continually developing more sophisticated epidemiological models to better understand how disease control resources can be applied more cost-effectively across the large population of cattle herds (Kao et al., 2006; Green et al., 2008; Tinsley et al., 2012). Cattle movements have received particular attention in recent years both because of their central role in the epidemiology of many economically important cattle diseases (Van Wuijckhuise et al., 1998; Alban et al., 2001; Gilbert et al., 2005) and because the movements of individual cattle have been explicitly recorded in a computerized database since 1998 (Mitchell et al., 2005). Using network based approaches, it has been consistently shown that targeting control measures at the small number of herds or movements that are highly connected in the trade network can lead to significantly greater reductions in disease prevalence than targeting the same number of herds or movements at random (Woolhouse et al., 2005; Rautureau et al., 2010; Volkova et al., 2010; Bajardi et al., 2011).

From a practical perspective, these findings must be interpreted with caution as most models assume that purchased cattle all carry the same risk of generating disease outbreaks in the destination herd. As numerous empirical studies have shown, the probability of any individual animal being infected or transmitting disease to susceptible cattle is strongly influenced by factors such as age, production type, and on-farm management practices (Daniels et al., 2002; Ohlson et al., 2010; Ramírez-Villaescusa et al., 2010; Carslake et al., 2011). For example, contagious mastitis pathogens are highly unlikely to spread through the movements of male cattle or store calves purchased for fattening, whereas older lactating dams are

predicted to have a significantly increased risk based on the higher prevalence of disease and greater opportunity to spread disease through contaminated milking equipment (Zadoks et al., 2001; Garcia Alvarez et al., 2011). It has also been suggested that larger herds are more likely to implement biosecurity measures to prevent disease introductions (Hoe and Ruegg, 2006) or to manage cattle in separate production groups (Caldow et al., 2005), which reduces the potential for subsequent within-herd and between-herd transmission.

Although there have been many descriptive studies on cattle movement networks (Bigras-Poulin et al., 2006; Ezanno et al., 2006; Aznar et al., 2011; Mweu et al., 2013), none to my knowledge have used these records to identify disease specific risk factors associated with the demographic characteristics of purchased cattle or to quantify the frequency with which these high risk movements occur in real world cattle movement networks. In this analysis, empirical data on bovine viral diarrhoea virus (BVDV) in Scottish cattle herds was used as a case study to illustrate the importance of accounting for demographic heterogeneity in network transmission models.

BVDV is an economically important pathogen for cattle producers worldwide because of its detrimental effects on herd productivity (Stott et al., 2003; Gunn et al., 2004; Varo Barbudo et al., 2008). During acute outbreaks, cattle infected with BVDV may exhibit non-specific clinical signs of depression, inappetence, fever, and diarrhoea leading to transient declines in milk production, growth performance, and animal fertility (Houe, 1995). More serious complications arise when BVDV crosses the placental barrier in pregnant cattle. Foetal infections have been associated with early embryonic death, abortions, stillbirths, congenital abnormalities, and the development of persistent infections in calves that gain immunotolerance to BVDV when exposed between days 43 and 120 of gestation. Persistently infected (PI) calves shed large quantities of virus for life and are primarily responsible for sustaining disease transmission at the population level (McClurkin et al., 1984; Lindberg and Houe, 2005). Due to underlying

immunosuppression and the development of fatal mucosal disease, few PI cattle survive beyond three years of age (Houe, 1992; Taylor et al., 1997). However, those that appear clinically normal are at risk of being sold to other herds as store cattle or breeding replacements leading to the exposure of pregnant dams at risk of generating additional PI calves (McClurkin et al., 1979; Muñoz-Zanzi et al., 2003; Bachofen et al., 2010). Numerous empirical studies have shown that purchasing PI replacement heifers and recovered cows carrying PI calves is associated with an increased risk of disease introductions, particularly since there are no available prenatal tests to determine the infection status of the foetus (Bitsch et al., 2000; Fray et al., 2000; Alban et al., 2001).

In this study, a network simulation model based on work by Tinsley and colleagues (Tinsley et al., 2012) is used to show the relative importance of replacement breeding cattle movements to the epidemiology of BVDV in Scotland. Then, an individual-based simulation model of within-herd BVDV transmission dynamics modified from work by Ezanno and colleagues (Ezanno et al., 2008) and parameterized directly from cattle movement records is used to predict the likelihood of specific types of replacement breeding cattle generating outbreaks in the destination herd. The findings are compared with serological data from surveyed beef suckler and herds to support model predictions. Finally, both the simulation data and serological data are used to explore the complex relationship between herd size and the risk of BVDV outbreaks.

Methods

Data sources

Serological data

A survey of 301 randomly selected beef suckler herds was performed in Scotland between October 2006 and September 2007 to estimate the national herd-level prevalence of BVDV (Brulisauer et al., 2010). During the farm visit, blood

samples were obtained from 10 randomly selected animals between 6 and 16 months of age (for 27 of the herds the number of animals sampled differed from 10, typically due to the group size being too small). The blood samples were processed using an indirect BVDV antibody ELISA to obtain antibody titres and were classified as positive or negative based on the percentage positivity (PP) score. Based on the two higher mixture distributions described previously for these data (Brulisauer et al., 2010), the 225 herds with less than 26.3% prevalence amongst young stock were considered control herds and the 76 herds with a within-group prevalence of more than or equal to 26.3%, were considered seropositive case herds.

A survey of 374 dairy herds was also performed in Scotland between October 2007 and May 2008 to estimate the prevalence of antibodies to BVDV in bulk tank milk samples (Humphry et al., 2012). The bulk milk tank samples were obtained through the farm's milk purchaser at the time of collection and processed using indirect BVDV antibody ELISA to obtain the percentage positivity (PP) score. Following the Swedish BVDV eradication class system, the 220 herds that did not vaccinate for BVDV were assigned into one of four groups based on their PP score. Class 0 herds were considered unlikely to have any seropositive animals indicating a low probability of BVDV infection, while Class 3 herds were considered highly likely to have many seropositive animals indicating a recent or active infection. For the purpose of this analysis, the 77 herds designated as Class 0 or Class 1 were considered control herds and the remaining 143 herds designated as Class 2 or Class 3 were considered seropositive case herds.

The questionnaire returned by the surveyed beef suckler and dairy farmers identified farms through the main postal address and so to link the serological results with records from the CTS database, attempts were made to match the farm address against a database of CPH codes provided by the Scottish government. Farms for which there was no available CPH code and farms for which there was an obvious discrepancy between the questionnaire estimates of herd size and CTS database estimates of herd size were excluded from the analysis. The final sample contained

255 beef suckler herds (67 case herds and 188 control herds) and 189 dairy herds (122 case herds and 67 control herds).

Cattle movement data

The Cattle Tracing System (CTS) database contains virtually complete records of the births, deaths, and movements of individual cattle in Great Britain since 2001 as well as information on sex, breed classification, and recorded calvings that can be used to determine the animal's production status at the time of movement. In this analysis, all records associated with cattle moved between Scottish farms from July 2004 through June 2007 were used to generate descriptive statistics on cattle movement patterns and to construct a dynamic contact network for performing disease simulations. After removing movements to and from locations classified as showgrounds or abattoirs, the data set included 1,355,416 individual cattle movements over the 3 year period.

Movement records for each farm are stored in the CTS database under a unique location identification number linked to the county-parish-holding (CPH) number used to register the farm for agricultural subsidy payments. For the purpose of this analysis, a farm was defined as any location classified as an agricultural holding or landless keeper (farmers housing cattle on rented land) with a Scottish county designation that housed cattle for at least one day during the study time period. Farms with at least 20 recorded beef breed calvings per year were classified as beef suckler herds and those with at least 20 recorded dairy breed calvings per year were classified as dairy herds. A small number of farms operating both beef suckler and dairy breeding herds with at least 20 recorded calvings each were classified as mixed production farms. Farms with fewer than 20 recorded calvings per year were considered small production herds, while farms with no recorded calvings were classified together as 'other' and likely included fattening units, seasonal grazing pastures, and temporary holding facilities.

Animal characterizations

The individual cattle movements were categorized based on the animals' demographic characteristics at the time of movement. To distinguish movements to and from seasonal grazing pastures from movements that represented cattle trade, a purchased replacement breeding heifer was defined as an animal that was born on a different location than the destination farm and subsequently calved on the destination farm. A purchased replacement breeding cow was defined as an animal that previously calved on a different location than the destination farm and subsequently calved on the destination farm. All male cattle and all female cattle that were slaughtered before 30 months of age without calving were grouped together as 'other' type cattle. Similarly, 'other' type cattle that were born on a different farm from the destination farm were considered purchased cattle.

The replacement breeding cattle were further subdivided into six production groups: open heifers, pregnant heifers, open dry cows, open lactating cows, pregnant dry cows, and pregnant lactating cows. An open breeding heifer was defined as a female animal with no previously recorded calvings that either subsequently delivered a calf or survived beyond 30 months of age and was greater than 280 days from the next recorded calving date. A pregnant breeding heifer was defined as a female animal with no previously recorded calvings that either subsequently delivered a calf or survived beyond 30 month s of age and was fewer than 280 days from the next recorded calving date. An open breeding cow was defined as a female animal with at least one prior calving and that was at least 280 days away from the next recorded calving date. A pregnant breeding cow was defined as a female animal with at least one prior calving and that was fewer than 280 days away from the next recorded calving date. Beef breed cows that were moved onto the farm at the same time as their calf were considered to be in lactation with a calf at foot, while those moved without a calf were considered to be dry cows. Dairy breed cows that were moved onto the farm within 305 days of the previous calving date were

also considered to be in lactation, while those moved greater than 305 days post-calving were considered to be dry cows.

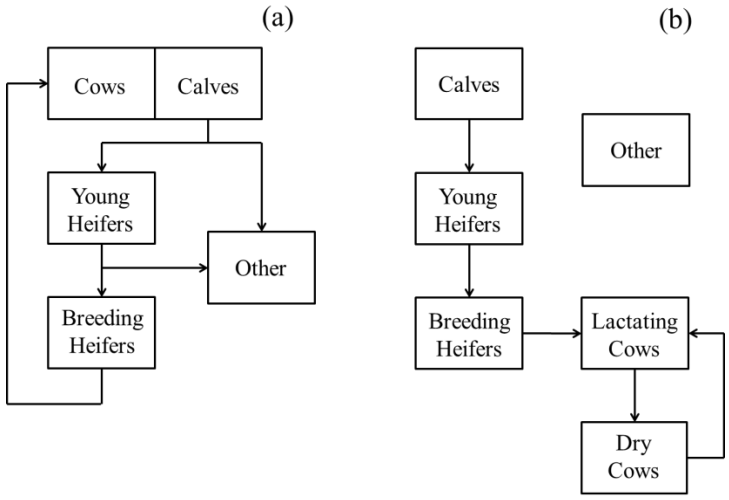
Within-herd simulation model

A stochastic individual-based simulation model was developed to explore the relative risk of purchased replacement breeding cattle causing outbreaks in the destination herd. The model included a demographic component to capture the typical management subgroups of Scottish beef and dairy herds, a seeding component to describe the introduction of BVDV through purchased replacement breeding cattle, and a disease component to describe the subsequent transmission of BVDV within and between management subgroups. The distribution of animals across the different management subgroups and movements on and off the farm were taken directly from CTS records to account for real world heterogeneity in herd demographic structure. This analysis focused on records from the 2,895 beef suckler herds and 546 dairy herds in Scotland with exclusively beef or dairy calvings that housed cattle continuously over the period from July 2004 through June 2007, that purchased at least one replacement breeding animal in the period from July 2004 through June 2005, and that had at least 20 recorded calvings. The simulation model was implemented in the C programming language.

Demographic component

Records for all cattle present in the study herds on 01 July 2004 were extracted from the CTS database. Each animal was initialized as a virtual object that carried information on its age, production subgroup, pregnancy status, and disease status at any given time point. Based on expert opinion from industry stakeholders on the typical management structure of Scottish beef suckler and dairy herds, animals were assigned into one of the production subgroups shown in Figure 8.1.

Figure 8.1: Diagrammatic representation of the production subgroups in typical Scottish (a) beef suckler and (b) dairy herds.



In beef suckler herds, all calves born in the herd remained with their dams until a fixed weaning age of 213 days (7 months). At weaning, male calves were transferred into the 'other' group and female calves were transferred into the 'young heifer' group. At the minimum age at first breeding for the farm, heifers that subsequently delivered a calf or survived beyond 30 months of age were transferred into the 'breeding heifer' group. All other heifers were assumed to be intended for fattening and transferred into the 'other' group. The minimum age at first breeding was calculated by taking the minimum age at first calving for heifers over the three year study period and subtracting the average gestation length of 280 days. Heifers remained in the 'breeding heifer' group until calving or until reaching 48 months of age. Given limitations in the CTS data, it was not possible to further separate animals into spring and fall calving units on farms with year-round calving patterns or to identify exposure to male cattle kept or purchased as breeding bulls.

In dairy herds, calves were removed from their dams immediately at birth. All male calves and crossbreed calves (defined as beef breed animals born to dairy breed dams) were transferred into the 'other' group. Female calves remained in the 'calf' group until a fixed age of 183 days (6 months) and were then transferred into

the 'young heifer' group until the minimum age at first breeding for the farm. Heifers remained in the 'breeding heifer' group until calving or until reaching 48 months of age. After calving, the dams were transferred to the 'lactating cow' subgroup until 42 days prior to the next calving, reflecting the average dry period for dairy cattle, or until more than 365 days into lactation if the animal failed to conceive. Animals remained in the 'dry cow' subgroup until the next record calving date or movement off the farm. An average gestation length of 280 days was again assumed.

On each day of the simulation, the herd demographic structure was updated in four steps: (1) animals within the herd were transitioned between production subgroups as appropriate, (2) animals were removed from the herd based on an event list of deaths and off-movements, (3) the pregnancy status of animals was updated based on an event list of breeding dates derived by subtracting 280 days from the next recorded calving date, and (4) animals were added to the herd based on an event list of births and on-movements.

Seeding component

From July 2004 through June 2005, the beef suckler herds collectively purchased 44,485 replacement breeding cattle, while the dairy herds collectively purchased 10,023 replacement breeding cattle. Each of these was treated as a separate disease seeding event. The animal's infection status at the time of purchase was determined stochastically through a series of binomial trials. The purpose was a relative weighting of the likelihood of the animal being infectious based on the known epidemiological features of BVDV.

First, each animal was assigned a probability of being PI based on its age. It was assumed that the average prevalence of PI cattle at birth was 3% and the probability of being PI decayed as an exponential function of age with a half-life of 365 days (Houe and Meyling, 1991; Houe et al., 1995b; Rüfenacht et al., 2000; Pillars and Groom, 2002; Fulton et al., 2009). If the animal was not PI, it was then assigned a random age of seroconversion generated from an exponential distribution

with a half-life of 1,095 days (Harkness et al., 1978; Luzzago et al., 1999; Talafha et al., 2009). The purpose was to account for the increasing probability that older cattle will have been previously exposed to BVDV either through natural exposure or immunization. Animals that were open and seronegative to BVDV at the time of purchase were assigned a 3% probability of being transiently infected. For animals that were purchased pregnant or with a calf at foot, it was assumed that if seroconversion occurred prior to the gestational risk period for generating a PI calf, then the calf would be born recovered with maternal antibodies. If the animal was still seronegative during the gestational risk period, it was assigned a 3% probability of giving birth to a PI calf. All calves born to pregnant PI dams were assumed to be PI and all animals that were transiently infected were assumed to be at the beginning of a 10 day infectious period.

Disease transmission component

The model for the within-herd transmission dynamics of BVDV following disease introduction was adapted directly from work by Ezanno and colleagues (2008). Disease was assumed to spread within and between production subgroups at the frequency-dependent rates described in Equation 1.

$$\lambda(g,t) = \beta_1 \frac{PI_g(t)}{N_g(t)} + \beta_2 \frac{TI_g(t)}{N_g(t)} + \sum_{a \neq g} \beta_3 \frac{PI_a(t)}{N_a(t)N_g(t)} \quad (1)$$

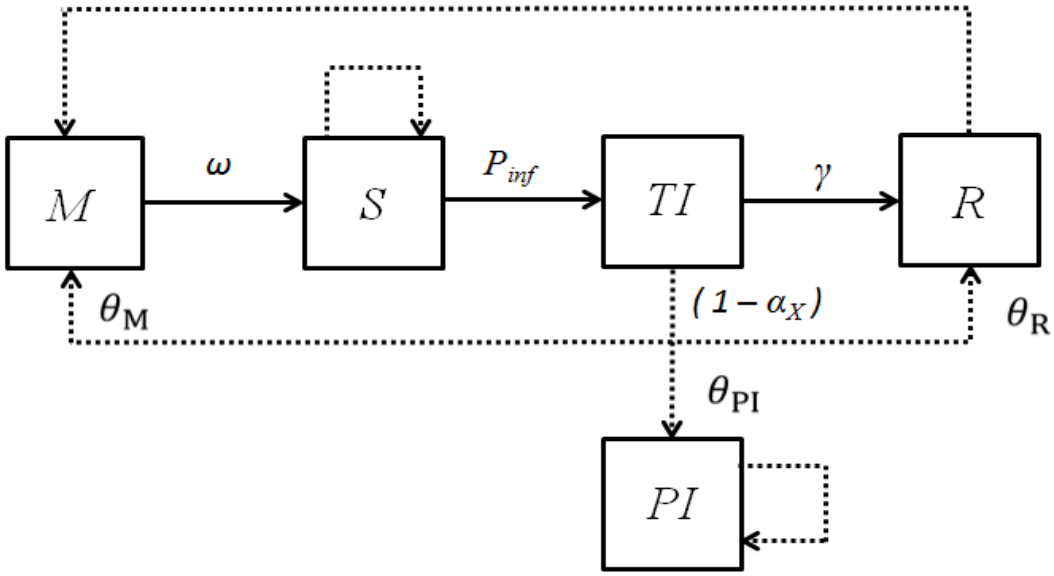
$$\rho_{inf}(g,t) = 1 - e^{-\lambda(g,t)} \quad (2)$$

where $X_g(t)$ is the number of animals in infectious state X within the same production subgroup at time (t), $X_a(t)$ is the number of animals in infectious state X in all other production subgroups at time (t), β_1 is the transmission rate from PI animals within the same production subgroup, β_2 the transmission rate from TI animals within the same production subgroup, β_3 the transmission rate from PI animals in all other production subgroups, N_g is equal to the total number of animals in the same production subgroup, and N_a is equal to the total number of animals in all other production subgroups.

Within each production subgroup, contact with both persistently infected (PI) and transiently infected (TI) animals was assumed to lead to possible virus transmission, while between production subgroups, only PI cattle were assumed to be able to transmit virus due to their much higher viral excretion rates. The probability of an individual animal acquiring BVDV (Equation 2) was updated on each day to reflect changes in the distribution of animals across production subgroups and infection states. All horizontal transmission resulted in the movement of cattle from the susceptible (S) state to the TI state. A diagrammatic representation of the mutually exclusive infection states is shown in Figure 8.2.

All TI cattle remained infectious for a period of 10 days (γ) before seroconverting and moving to the recovered (R) state. Immunity to BVDV was assumed to be lifelong. For S dams infected during early gestation (days 0 to 42), there was a probability α_e of embryonic loss or abortion. For S dams infected during mid-gestation (days 43 to 150), there was a probability $\alpha_m$of abortion and if the calf survived, a probability θ_{PI} of being PI, a probability θ_{R} of being R, and a probability θ_{M} being born protected by maternal antibodies (M). Temporary immunity to BVD through maternal antibodies was assumed to last for 183 days (ω) after which the animal joined the S group. All dams infected during early gestation (days 1 to 42) and late gestation (days 151 to 280) gave birth to M calves, all PI dams gave birth to PI calves, and all S dams gave birth to S calves. Given the short duration of the model, it was assumed that there was no increase in mortality amongst PI calves.

Figure 8.2: Diagrammatic representation of the progression of animals through mutually exclusive disease states for BVDV. The dotted lines indicate the immunological status of calves born to dams in disease state X.



Variable	Definition	Value
M	Calf protected by maternal antibodies	-
S	Susceptible animal	-
TI	Transiently infected animal	-
PI	Persistently infected animal	-
R	Recovered or immune animal	-
ω	Duration of maternal immunity (days)	183[1]
P_{inf}	Probability of infection (per day)	Eq. 2[3]
β_1	Within-group transmission rate from PI animals (per day)	0.5[3]
β_2	Within-group transmission rate from TI animals (per day)	0.03[2]
β_3	Between-group transmission rate from PI animals (per day)	0.1[2]
γ	Recovery period for TI animals (days)	10[1]
Early gestation (days 1 to 42)		
α_e	Probability of abortion during early gestation	0.80[3]
α_m	Probability of abortion during mid-gestation	0.25[3]
θ_{PI}	Probability giving birth to PI if infected during mid-gestation	0.934[3]
θ_{M}	Probability giving birth to M if infected during mid-gestation	0.033[3]
θ_R	Probability giving birth to R if infected during mid-gestation	0.033[3]

1. (Innocent et al., 1997) 2. (Viet et al., 2004) 3. (Ezanno et al., 2007)

Simulation conditions

A total of 1,000 replicates were performed for each seeding event. Each simulation started on 01 July2004 with all animals in the herd assumed to be susceptible. The demographic structure of the herd was updated on a daily basis until the seeding date, after which the model was allowed to run for an additional 730 days. All cattle subsequently moved onto the farm were assumed to be susceptible. The outcome measure for each simulation was a binary response variable of whether or not the purchased animal caused at least one additional dam in the herd to generate a PI calf over the two year period.

Between-herd simulation model

The individual movements of cattle from July 2004 through June 2007 were used to generate a dynamic contact network to assess the impact of replacement breeding cattle movement on BVDV transmission dynamics. For each movement, the departure location, destination location, and date were recorded. Movements that occurred through livestock markets were treated as direct movement between farms by pairing the movement onto the market location with the corresponding movement off the market location. Cross border movements and movements to abattoirs or showgrounds were excluded so that the network was closed.

A simple SIS model based on published work by Tinsley and colleagues was used to describe the transmission dynamics of BVDV through the network of farms (Tinsley et al., 2012). At the beginning of each simulation, disease was seeded on 1,000 farms at random on 01 July 2004. Each infected farm was assigned an infectious period drawn at random from an exponential distribution with a half-life of 3 years (1095 days) (Viet et al., 2004; Tinsley et al., 2012). The infection status of individual farms and movements between them were then updated on a daily basis. Each individual animal moved off an infected farm had a 0.016 probability of transmitting BVDV to a susceptible destination farm based on the approximate prevalence of PI cattle in infected herds (Cherry et al., 1998; Viet et al., 2004;

Tinsley et al., 2012). The network 'edges' between farms were therefore weighted by the number of cattle moved. Each susceptible farm that became infected was also assigned an infectious period at random and farms that reached the end of their infectious period reverted back to a susceptible state. To ensure adequate time for the system to reach steady state equilibrium, the simulation was allowed to run for a total of 50 years by recycling the 3 year movement data set. Endemic prevalence was measured as the average number of farms infected on any given day over the last 3 years of the simulation.

A targeted removal approach was used to assess the relative importance of replacement breeding cattle movements to network transmission dynamics (Rautureau et al., 2010). At the beginning of each simulation, a proportion of replacement breeding cattle movements were removed from the network data set at random. The simulation was then run on the reduced movement network to monitor changes in the predicted endemic prevalence. In a real world setting, this would correspond to testing purchased replacement breeding cattle to ensure that none were PI or carrying a PI calf and thereby effectively removing the movement from the network. A total of 10,000 simulations were performed with the proportion to be removed drawn at random from a uniform distribution bounded at 0 and 1 to represent no removal and complete removal, respectively. As a benchmark for comparison, another 10,000 simulations were performed where an equivalent number of random movements were removed from the network data set ignoring the production type of cattle. The results from both simulation sets were plotted as the percentage of total network movements removed against the percentage change in endemic prevalence using the maximum recorded value for endemic prevalence amongst the simulations as the baseline value.

An additional 10,000 replicates were run on the full movement network for use in the herd size analysis. The total number of times an individual farm was actively infected at the end of each simulation was recorded.

Statistical analyses

Descriptive statistics

Detailed descriptive statistics on features of the cattle movement network relevant to BVDV epidemiology were provided. These included the demographic characteristics and movement patterns of breeding herds, the frequency distribution of replacement breeding cattle movements, the age of replacement breeding heifers relative to the age at first calving, the gestational stage of pregnant cattle, and the age at first off movement for beef and dairy calves.

Within-herd simulation model

The results from the within-herd simulation models were analyzed using mixed effects generalized linear models (GLM) with a binomial distribution. Data from the beef suckler herds were analyzed separately from the dairy herds due to inherent differences in management practices. The response variable was the counts of successes and failures for each seeding event and the predictor variable was the seeding event type (open heifer, pregnant heifer, open dry cow, open lactating cow, pregnant dry cow, or pregnant lactating cow). Herd was included as a random effect to account for covariance between observations on the same farm. The results from the regression model were reported as odds ratios (ORs) with the corresponding 95% confidence intervals (CIs).

Data from the 255 surveyed beef suckler herds and 189 surveyed dairy herds were used to provide empirical support for the simulation model findings. For each herd, the total number of cattle purchased in the two year period prior to serological sampling was recorded. A series of six binary categorical variables were created representing each of replacement breeding cattle types. The levels of the variables were “None purchased” and “At least one purchased”. Herds that purchased no cattle in the 2 year period prior to sampling were considered closed herds. The odds of a closed herd being seropositive for BVDV were initially calculated and the

remaining analyses then focused on the subset of 233 open beef suckler herds and 150 open dairy herds.

Preliminary univariate screens were performed to select variables for inclusion in the final multivariate logistic regression models. Variables that were associated with BVDV seropositivity at a p-value < 0.20 were retained. Thereafter, components of the final multivariate models were determined by a backwards stepwise elimination process in which variables with the highest p-values were sequentially dropped from the model until all the remaining variables had a p-value < 0.05. Forwards stepwise selection was then performed adding in each of the eliminated variables in turn and checking for p-values of < 0.05 to ensure that no variables were excluded based on the order of elimination.

Between-herd simulation model

The results from the between-herd simulation model were used to explore the relationship between herd size and the risk of a herd becoming infected with BVDV through cattle movements. Average farm size was estimated by dividing the total number of animal days recorded for the location in the CTS Population data table over the three year period by 1,095. Quadratic GLM models with a binomial distribution fit to the counts of successes and failures were used to assess linearity in the relationship between herd size and BVDV risk. The herd size variable was log transformed and centralized prior to analysis. Correlations between the linear and quadratic terms were checked to rule out collinearity.

A similar framework was used to evaluate the relationship between seropositivity and herd size in the surveyed beef suckler and dairy herds, except the response variable in this case was binary. The predicted probabilities for both sets of regression models were plotted against herd size to illustrate the nature of the non-linear relationships.

Results

Network descriptive statistics

From July 2004 through June 2007, there were 1,355,416 individual cattle movements between the15,809 active Scottish cattle farms. Basic descriptive statistics on the movement patterns and demographic characteristics of these herds are presented in Table 8.1. The vast majority of herds were open with 71.9% beef suckler herds, 59.5% of dairy herds, 68.8% of mixed breeding herds, and 50.1% of small breeding herds introducing at least one replacement breeding animal over the three year period.

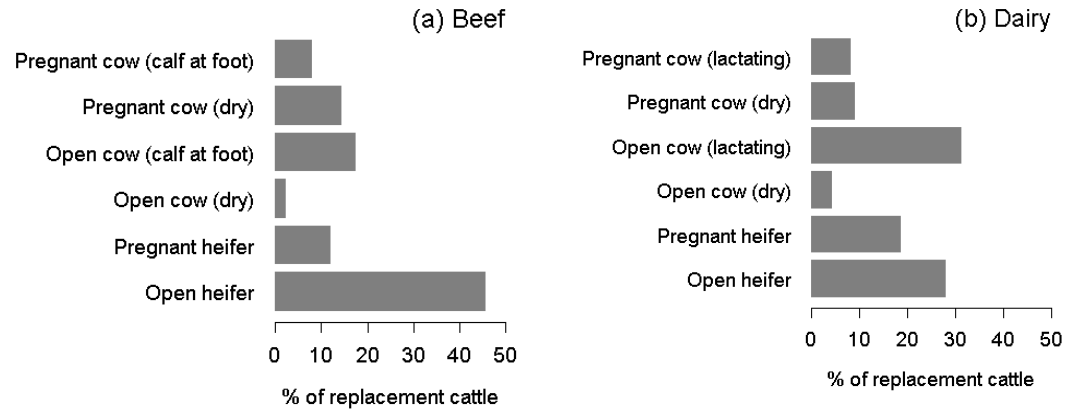
Only 22 of the 255 surveyed beef suckler herds (9%) and 39 of the 189 surveyed dairy herds (21%) remained completely closed to cattle movements in the two year period prior to serological testing. This practice was associated with a significantly decreased odds of being seropositive for BVDV (OR: 0.12, 95% CI: 0.01 – 0.60, p = 0.041 for beef suckler herds and OR: 0.38, 95% CI: 0.18 – 0.78, p = 0.008 for dairy herds). Amongst the open herds, beef suckler herds that purchased replacement breeding cattle had a 2.09 times greater odds of being seropositive for BVD (95% CI: 1.06 – 4.39, p = 0.040) compared with herds that purchased store cattle only. Similarly, open dairy herds that purchased replacement breeding cattle were 2.67 times more to be seropositive for BVDV (95% CI: 1.32 – 5.52, p = 0.006) than open herds that purchased store cattle only.

Table 8.1: Descriptive statistics on farm demographic characteristics and total number of cattle movements by production type from July 2004 through June 2007.

			Percentiles		
	% of herds with movements	Mean	10th	50th	90th
Beef suckler herds (N = 5,378)					
Average number of calvings per year	-	78	26	58	150
Average total herd size	-	220	69	164	424
Total number of cattle movements	95.1 %	91	2	25	178
Replacement breeding cattle	71.9 %	27	2	15	62
Dairy herds (N = 1,293)					
Average number of calvings per year	-	113	44	97	190
Average total herd size	-	328	137	293	539
Total number of cattle movements	86.7 %	73	1	15	155
Replacement breeding cattle	59.5 %	34	2	16	77
Mixed breeding herds (N = 160)					
Average number of calvings per year	-	147	72	120	230
Average total herd size	-	453	204	378	752
Total number of cattle movements	93.1 %	163	2	38	322
Replacement breeding cattle	68.8 %	71	4	32	122
Small breeding herds (N = 5,112)					
Average number of calvings per year	-	7	1	5	17
Average total herd size	-	34	3	19	66
Total number of cattle movements	75.2 %	78	1	6	124
Replacement breeding cattle	50.1 %	6	1	3	15
Other type herds (N = 3,866)					
Average total herd size	-	32	1	4	94
Total number of cattle movements	64.9 %	185	2	43	456

An estimated 12.1% of all individual cattle movements were attributable to replacement breeding cattle trade. Open heifers were the most common type of replacement breeding cattle purchased by beef suckler herds, while open cows in lactation were the most common type for dairy herds (Figure 8.3). Overall, 25.6 % of beef replacements were sold with a calf at foot and 40.5 % of dairy replacements were sold in lactation.

Figure 8.3: Distribution of replacement (a) beef and (b) dairy breeding cattle by parity and physiological status.



As illustrated in Figure 8.4, there were distinct differences in the age of replacement beef and dairy heifers at the time of purchase. For beef heifers, there was a large peak in movements shortly after birth with smaller peaks occurring approximately every 6 months thereafter. The majority of beef heifers purchased under 6 months of age (69.1%) were crossbreed calves from dairy herds. Most beef heifers were purchased well in advance of their first calving date. For dairy heifers, there was a single large peak in movements at 30 months of age coinciding with the peak in age at first calving.

Of the 34.9% of beef dams that were purchased pregnant, 12.3% were in early gestation, 36.3% were in mid gestation, and 51.3% were in late gestation (Figure 8.5). Of the 38.5% of dairy dams that were purchased pregnant, 9.4% were in early gestation, 23.0% were in mid gestation, and 67.6% were in late gestation.

Over 90% of beef calves were moved off the birth farm by 30 months of age with peaks in the frequency of movements at approximately 3, 7, 12, and 18 months of age (Figure 8.6). In contrast, dairy calves had a sharp peak in the frequency of movements shortly after birth with over 20% moved off the birth farm by 1 month of age.

Figure 8.4: Age distribution of replacement breeding heifers at the time of purchase and average age at first calving for (a) beef breed cattle and (b) dairy breed cattle. Note the x axes have been truncated at 50 months

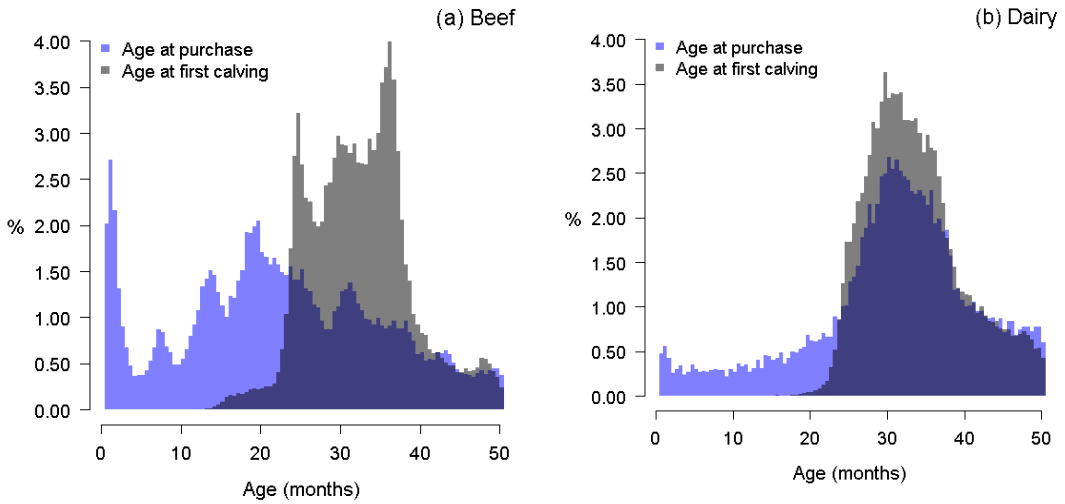
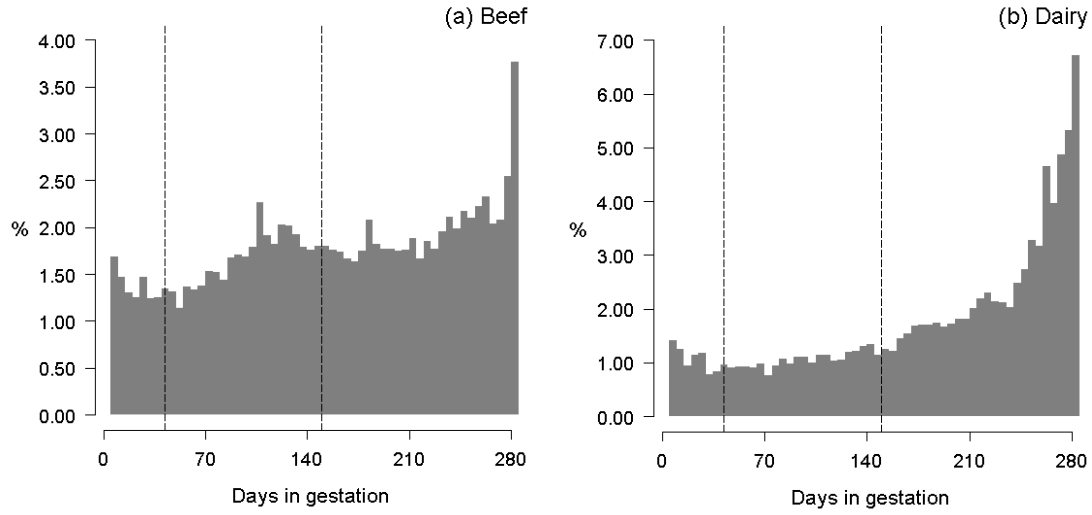


Figure 8.5: Distribution of the number of days in gestation of pregnant replacement (a) beef and (b) dairy cattle at the time of purchase. The vertical lines indicate the divisions into early, mid, and late gestation.



The movements of replacement breeding cattle had a disproportionately strong influence on network transmission dynamics (Figure 8.7). Removing 1% of cattle movements at random resulted in an approximately 0.8 % reduction in endemic prevalence, while removing the equivalent number of replacement breeding

cattle movements resulted in an approximately 2.9 % reduction in endemic prevalence. The maximum achievable reduction in endemic prevalence by removing all replacement breeding cattle movements was 44.7% compared with 23.4% when movements were targeted at random.

Figure 8.6: Distribution of the ages of (a) beef and (b) dairy cattle at the time of first off movement from the birth farm. Note the x-axes have been truncated at 30 months.

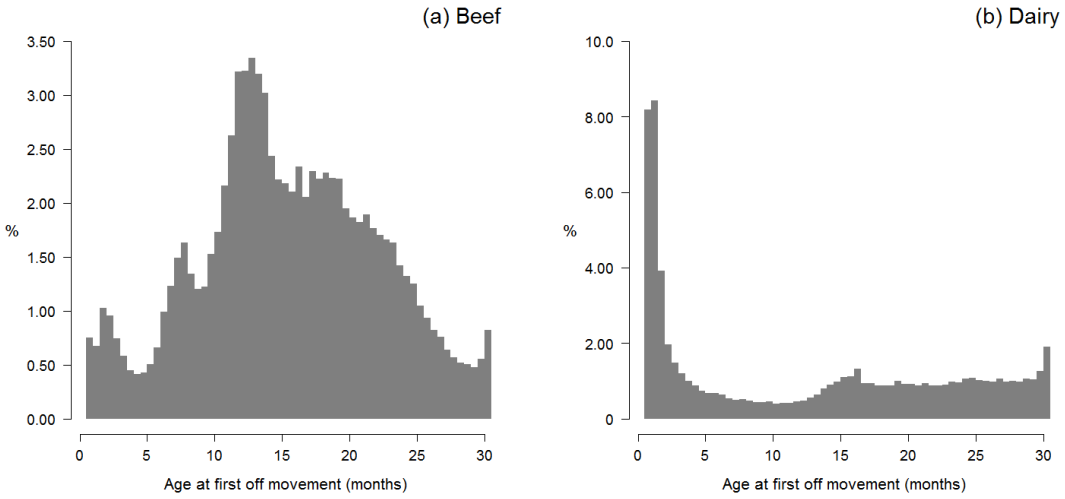
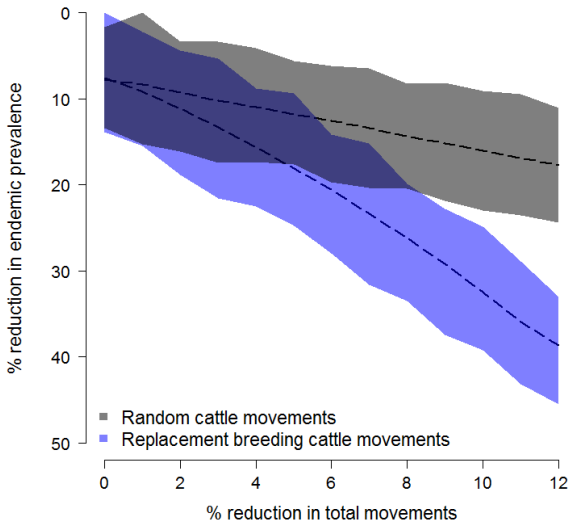


Figure 8.7: Predicted change in the endemic prevalence of BVDV following targeted removal of replacement breeding cattle movements and random removal of cattle movements. The range from 10,000 simulation replicates is shown.



Within-herd simulation model

Results from the within-herd simulation model predicted that the risk of replacement breeding cattle movements generating additional PI calves in the receiving herd varied based on the animal production type and physiological status (Table 8.2). Compared with the movements of open beef heifers, the movements of pregnant beef heifers had 1.76 times greater odds (95% CI: 1.74 – 1.77, $p < 0.001$) of generating additional PI calves and the movements of open beef cows with a calf at foot had 1.23 times greater odds (95% CI: 1.22 – 1.24, $p < 0.001$) . For dairy herds, the movements of open heifers had the greatest odds of generating additional PI calves compared with all other animal production types. The movements of open dry cows had the lowest risk for both beef suckler and dairy herds, although these movements were relatively infrequent.

Table 8.2: Theoretical risk of generating additional PI calves associated with the production type of replacement breeding cattle purchased by open (a) beef suckler herds and (b) dairy herds based on within-herd simulation data.

	N	OR	95% CI	p-value
(a) Beef suckler herds				
Open heifers	22,473	Ref	-	< 0.001
Pregnant heifers	5,205	1.76	1.74 – 1.77	< 0.001
Open cows (dry)	1,184	0.13	0.12 – 0.13	< 0.001
Open cows (calf at foot)	8,269	1.23	1.22 – 1.24	< 0.001
Pregnant cows (dry)	5,131	0.68	0.67 – 0.79	< 0.001
Pregnant cows (calf at foot)	2,176	0.94	0.92 – 0.95	< 0.001
(b) Dairy herds				
Open heifers	3,188	Ref	-	< 0.001
Pregnant heifers	1,734	0.92	0.90 – 0.93	< 0.001
Open cows (dry)	275	0.44	0.42 – 0.46	< 0.001
Open cows (lactating)	3,510	0.67	0.66 – 0.68	< 0.001
Pregnant cows (dry)	547	0.64	0.62 – 0.66	< 0.001
Pregnant cows (lactating)	769	0.68	0.67 – 0.70	< 0.001

Similar findings were observed using empirical serology data from the surveyed beef suckler and dairy herds. Open beef suckler herds that purchased pregnant heifers, open cows with a calf at foot, and pregnant dry cows were at significantly increased risk of being seropositive for BVDV in the univariate

analyses (Table 8.3). In the multivariate model, only the former two variables remained significant. The odds of a beef suckler herd being seropositive for BVDV were 2.18 times greater with the purchase of pregnant heifers (95% CI: 1.17 – 4.08, p = 0.014) and 2.09 times greater with the purchase of open cows with a calf at foot (95% CI: 1.13 – 3.88, p = 0.018). For open dairy herds, the odds of being seropositive for BVDV increased with the purchase of open heifers, open dry cows, and open lactating cows in the univariate analysis (Table 8.3). However, when combined in the multivariate model, only the purchase of open heifers remained a significant predictor at the 0.05 level.

Table 8.3: Univariate analysis of risks for BVDV seropositivity associated with the production type of replacement breeding cattle purchased by open (a) beef suckler herds and (b) dairy herds.

		Cases	Controls	OR	95% CI	p-value
(a) Beef suckler herds						
Open heifers	No	26	84	Ref	-	-
	Yes	40	83	1.56	0.88 – 2.81	0.134
Pregnant heifers	No	34	124	Ref	-	-
	Yes	32	43	2.74	1.50 – 4.94	< 0.001
Open cows (dry)	No	50	141	Ref	-	-
	Yes	16	26	1.73	0.85 – 1.74	0.123
Open cows (calf at foot)	No	29	112	Ref	-	-
	Yes	37	55	2.60	1.45 – 4.69	0.001
Pregnant cows (dry)	No	38	135	Ref	-	-
	Yes	28	32	3.11	1.67 – 5.81	< 0.001
Pregnant cows (calf at foot)	No	49	129	Ref	-	-
	Yes	17	38	1.18	0.59 – 2.25	0.627
(b) Dairy herds						
Open heifers	No	50	34	Ref	-	-
	Yes	54	12	3.06	1.46 – 6.77	0.004
Pregnant heifers	No	61	32	Ref	-	-
	Yes	43	14	1.61	0.78 – 3.45	0.206
Open cows (dry)	No	82	43	Ref	-	-
	Yes	22	3	3.84	1.24 – 16.9	0.036
Open cows (lactating)	No	54	33	Ref	-	-
	Yes	50	13	2.35	1.13 – 5.10	0.025
Pregnant cows (dry)	No	82	39	Ref	-	-
	Yes	22	7	1.49	0.61 – 4.05	0.398
Pregnant cows (lactating)	No	78	39	Ref	-	-
	Yes	26	7	1.86	0.77 – 4.98	0.187

Between-herd simulation model

The between-herd simulation model was used to estimate the probability of individual herds being infected with BVDV at endemic equilibrium over 10,000 simulation replicates. Based strictly on the volume and frequency of cattle movements, larger beef suckler and dairy herds had significantly greater odds of being infected with BVDV. The regression coefficients from the fitted quadratic regression models are shown in Table 8.4 and plots of the predicted probabilities against herd size are shown in Figure 8.8.

In contrast, the quadratic logistic regression models fitted against the empirical serology data predicted that beef suckler herds at the lower and upper limits of the herd size range were at significantly decreased risk of being seropositive for BVDV. There was no significant relationship between herd size and the risk of being seropositive for BVDV amongst dairy herds. The regression coefficients from the fitted quadratic regression models are shown in Table 4 and plots of the predicted probabilities against herd size are shown in Figure 8.9.

Table 8.4: Quadratic logistic regression models for (a) beef suckler herds and (b) dairy herds showing the effect of the centralized log transformed herd size (expressed as a quadratic polynomial) on the odds of being seropositive for BVD

Variable	Coefficient	SE	z	p-value
(a) Beef suckler herds				
Centralized $\log_{10}$(Herd size)	2.181	0.002	1144	< 0.001
Centralized $\log_{10}$(Herd size)^2	-0.769	0.004	-187	< 0.001
(b) Dairy herds				
Centralized $\log_{10}$(Herd size)	1.317	0.005	241	< 0.001
Centralized $\log_{10}$(Herd size)^2	1.636	0.015	106	< 0.001

Figure 8.8: Predicted probability of a (a) beef suckler herd or (b) dairy herd being infected at endemic equilibrium on the basis of regression models fitted against quadratic polynomial for the log transformed herd size.

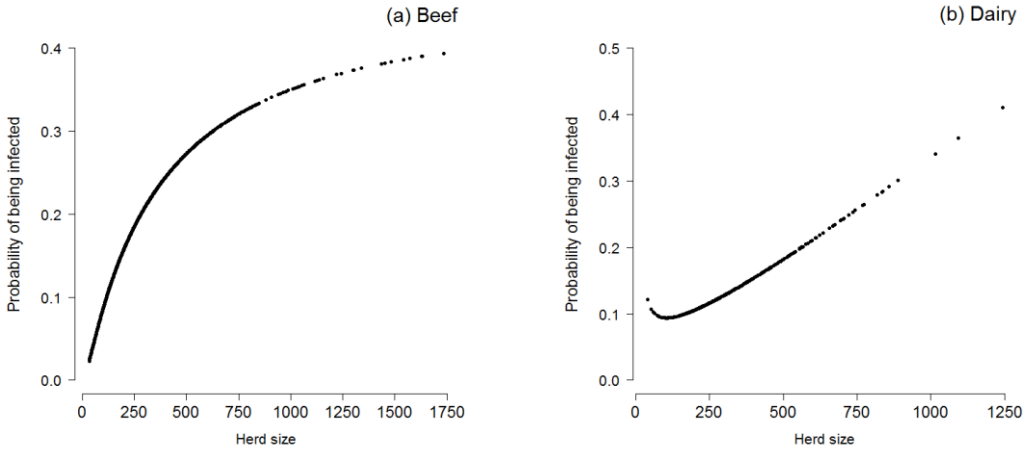
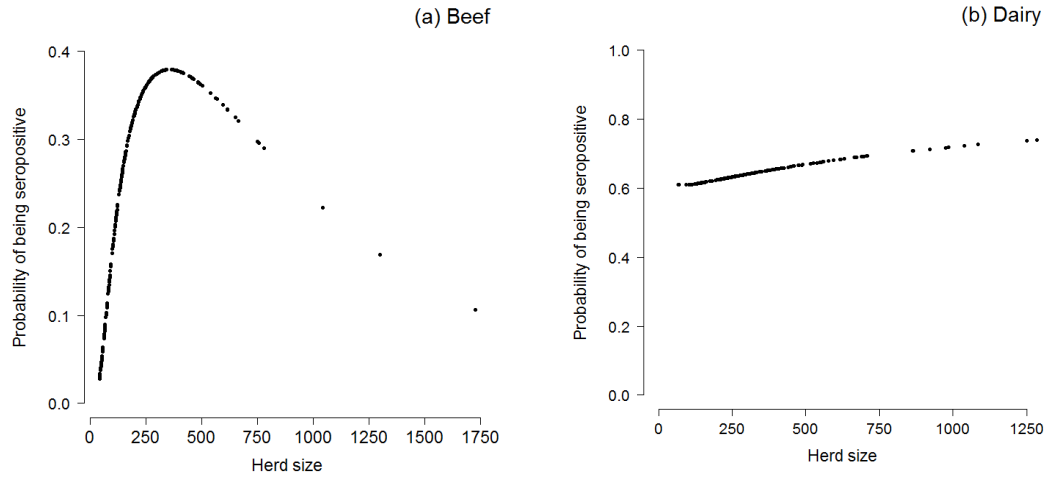


Table 8.5: Quadratic logistic regression models for (a) beef suckler herds and (b) dairy herds showing the effect of the centralized log transformed herd size (expressed as a quadratic polynomial) on the odds of being seropositive for BVDV.

Variable	Coefficient	SE	z	p-value
(a) Beef suckler herds				
Intercept	-0.727	0.174	-4.189	
Centralized $\log_{10}$(Herd size)	2.012	0.589	3.414	< 0.001
Centralized $\log_{10}$(Herd size)^2	-3.811	1.401	-2.720	0.007
(b) Dairy herds				
Intercept	0.597	0.164	3.639	
Centralized $\log_{10}$(Herd size)	0.634	0.585	0.585	0.278
Centralized $\log_{10}$(Herd size)^2	-0.394	1.073	1.073	0.714

Figure 8.9: Predicted probability of a (a) beef suckler herd or (b) dairy herd being seropositive for BVDV on the basis of the logistic regression models fitted against quadratic polynomial for the log of herd size.



Discussion

Results from this study demonstrate how the basic records of individual births, deaths, and movements available through national cattle movement databases can be used to quantify disease specific risk factors for endemic diseases and to

determine the relative importance of high risk movements to disease transmission dynamics at the population level. Although BVDV was used as an example, the basic principles and methodologies are equally relevant to the many other endemic cattle diseases that spread through cattle movement networks, such as bovine tuberculosis, bovine paratuberculosis, bovine herpesvirus 1, bovine leukaemia virus, *Escherichia coli* O157, and contagious mastitis.

Similar to other empirical risk factor analyses (Valle et al., 1999; Mainar-Jaime et al., 2001; van Schaik et al., 2002), there was strong evidence that purchasing cattle of any production type significantly increased the odds of being seropositive for BVDV. However, it was also shown that not all cattle movements carry the same risk of generating outbreaks in the receiving herd. From a theoretical perspective, the movements of purchased replacement breeding cattle were responsible for only 12% of all individual cattle movements yet had a disproportionately strong influence on the risk of disease spreading through the Scottish cattle movement network. This suggests that there is something unique about the network properties of herds that buy and sell replacement breeding cattle that may be increasing the risk of disease introductions. A recent study from Sweden found that herds with large ingoing infection chains (a measure which accounts for both the number and connectivity of source herds for purchased cattle) were significantly more likely to be seropositive for bovine coronavirus and bovine respiratory syncytial virus than more isolated herds (Frössling et al., 2012). With the limitations of the small study sample, it was not possible to investigate whether herds that sold replacement breeding cattle were more likely to be seropositive for BVDV and whether placing increased biosecurity restrictions on herds that sell replacement breeding cattle would be a more cost-effective control strategy. These questions may be answered in the near future as more comprehensive surveillance data from the recently launched Scottish BVD Eradication Scheme becomes available (Anonymous, 2013).

Both the within-herd simulation model and empirical data provided evidence that pregnant beef heifers, open beef cows sold with a calf at foot, and open dairy heifers were at increased risk of causing disease outbreaks compared with other categories of replacement breeding cattle. These findings reflect the combined probability of the animal being PI or carrying a PI calf and being introduced to the herd when susceptible cattle were in the gestational risk period for generating additional PI calves. Pregnant replacement cattle represent a particular epidemiological challenge for beef suckler herds since there are no reliable prenatal diagnostic tests to identify animals carrying a PI calf and once born, the calves mix directly with susceptible breeding dams until weaning at approximately 6 to 8 months of age (Fray et al., 2000). Given that the majority of farmers do not routinely perform diagnostic testing at the time of purchase, it is unlikely that these calves are tested after birth to identify and remove PIs (Negrón et al., 2011; Brennan and Christley, 2012). In contrast, the purchase of pregnant cattle was not a significant risk factor for BVDV seropositivity in dairy herds. The most likely explanation is that dairy calves are removed from their dams within 24 hours of birth and either sold directly to fattening units for beef production or raised in separate production units on the farm. Therefore, even if a pregnant replacement dam gives birth to a PI calf, there are fewer opportunities for disease to spread to susceptible breeding cattle.

Contrary to expectations, the purchase of open beef replacement heifers was not a significant risk factor for BVDV seropositivity in the empirical analysis. One possible explanation is that beef heifers were purchased at a much younger age than dairy heifers and under certain circumstances, it has been shown that exposing susceptible heifers to PI cattle can be beneficial in inducing protective immunity against transient BVDV infections during early gestation (Innocent et al., 1997). The possibility that the movement variables were proxies for other herd management practices associated with a greater risk of BVDV also cannot be ruled out. For example, herds that are actively infected with BVDV may need to purchase

replacement breeding to compensate for the negative effects on fertility and reproductive performance (David et al., 1994; Fredriksen et al., 1998; Rüfenacht et al., 2001). As highlighted by Lindberg and Alenius (1999), the purchase of susceptible breeding replacement cattle at risk for generating PI calves may contribute to the persistence of BVDV in these herds. This is an important consideration for national control programmes that focus primarily on preventing infected animals from entering susceptible breeding herds.

Previous analyses have identified herd size as a risk factor for BVDV seropositivity with the proposed mechanisms being the greater frequency of direct and indirect contacts with other herds and the greater number of pregnant dams at risk for generating PI calves (Houe et al., 1995a; Mockeliūniene et al., 2004; Lindberg and Houe, 2005; Ersbøll et al., 2010; Cowley et al., 2012; Sarrazin et al., 2013). In this study, the between-herd simulation model predicted that larger herds were more likely to be infected simply based on the volume and frequency of cattle movements alone. However, the empirical data showed that the relationship between herd size and seropositivity was non-linear for beef suckler herds and non-significant for dairy herds. This provides further evidence that simple network simulation models fail to capture epidemiologically important features of within-herd and between-herd transmission dynamics. The non-linear relationship observed for beef suckler may be explained by the increased likelihood of larger herds managing animal in separate production groups. Theoretical work by Ezzano and colleagues (2007, 2008) has shown that this practice reduces outbreak severity in dairy herds due to the lower probability of on-farm transmission and it likely that the same principles apply to beef suckler herds. It has also been suggested that larger livestock herds have higher biosecurity standards in general because of the greater potential costs associated with disease outbreaks (Hoe and Ruegg, 2006). Although the results are not shown here, there was evidence that larger beef suckler herds were significantly more likely to purchase cattle from accredited BVDV free herds.

The interpretation for dairy herds is complicated by the use of bulk milk tank testing to identify seropositive herds. Whereas the presence of antibodies in young stock most likely indicates a recent or active BVDV infection, antibodies in bulk tank milk can remain elevated for months to years after an outbreak depending on the rate that seroconverted cattle are removed from the lactating herd (Ståhl et al., 2008; Booth et al., 2013). Therefore, recent movement patterns may not be a good predictor of seropositivity in these herds. There were also limitations in how the CTS data were used to define animal production types and epidemiologically relevant cattle movements. For example, it was not possible to distinguish heifers that were purchased as store cattle for fattening from those that were purchased as replacement breeding animals, but culled prior to calving. This may have underestimated the number of herds that purchased replacement breeding cattle as well as the potential risk associated with open heifers. Known temporary movements from locations such as showgrounds or seasonal grazing pastures were also excluded since these do not represent a direct transfer of ownership. However, these as well as other mechanisms of local spread may be important risk factors for BVDV outbreaks (Bitsch et al., 2000; Ersbøll et al., 2010; Truyers et al., 2010).

To my knowledge, only one other published study to date has used demographic records from the CTS database to explicitly model the heterogeneous patterns in cattle births, deaths, and movements for individual herds (Carslake et al., 2011). Although these models are challenging to parameterize due to the lack of empirical data on within-herd structure and transmission dynamics, they represent an important direction for future epidemiological research. The motivation for individual farmers to participate in voluntary disease control programmes is often based on the perceived risk of disease introductions as wells as the potential financial impact of disease outbreaks (Billinis et al., 2005; Toma et al., 2013). By tailoring within-herd models to the farm's unique management situation, it is possible to provide farmers, veterinarians, and policy makers with better guidance on the optimal strategies for disease control and prevention. These models can also

be linked with traditional network simulation models to explore issues such as the effects of animal and herd demographic characteristics on the sensitivity and specificity of national disease surveillance programmes.

Conclusion

Modelling the spread of endemic diseases through cattle movement networks requires a good understanding of the individual animal and farm characteristics that contribute to the risk of disease transmission. Findings from this study demonstrate that simple network transmission models fail to capture many epidemiologically important features of endemic disease dynamics such as the risk of individual animals being infected based on their age and production type or the risk of disease spreading to susceptible cattle based on the destination herd's biosecurity and management practices. Although existing information in the CTS database can be used to enhance future epidemiological models, there is a strong need for more comprehensive herd-level and industry-level data to validate the model assumptions and predictions.

Chapter 9

Impact of changes in movement testing legislation on the risks of bovine tuberculosis[3]

Summary

Legislation requiring the pre- and post-movement testing of cattle imported to Scotland from regions with high bovine tuberculosis (bTB) incidence was phased in between September 2005 and May 2006 as part of efforts to maintain Officially Tuberculosis Free (OTF) status. In this analysis, centralized cattle movement records were used to investigate the influence of the legislative change on import movement patterns and the movement-based risk factors associated with new bTB herd breakdowns identified through routine testing or slaughter surveillance. The immediate reduction in the number of import movements from high incidence regions of England and Wales into Scotland suggests that pre- and post-movement testing legislation has had a strong deterrent effect on cattle import trade. Combined with the direct benefits of a more stringent testing regime, this likely explains the observed decrease in the odds of imported cattle subsequently being identified as reactors in herd breakdowns detected through routine surveillance compared to Scottish cattle. However, at the farm-level, herds that recently imported cattle from high incidence regions were still at increased risk of experiencing bTB breakdowns, which highlights the delay between the introduction of disease control measures and detectable changes in incidence. With the relative infrequency of routine herd tests and the insidious nature of clinical signs, past import movements were likely still important in determining the present farm-level risk for bTB breakdown. However, the possibility of low level transmission between Scottish cattle herds cannot be ruled out given the known issues with test sensitivity, changes in import animal

[3] This chapter is a modified version of the following publication: Gates, M.C., Volkova, V.V., Woolhouse, M.E.J., 2013. Impact of changes in cattle movement regulations on the risks of bovine tuberculosis for Scottish farms. Preventive Veterinary Medicine 108, 125-136.

demographics, and the potential for on-farm transmission. Findings from this analysis emphasize the importance of considering how farmer behavioural change in response to policy interventions may influence disease transmission dynamics.

Introduction

The incidence of bovine tuberculosis (bTB) varies across the European Union with certain countries recognized as Officially Tuberculosis Free (OTF) under the provisions of Council Directive 64/432/EEC. This includes Scotland since September 2009. OTF status does not imply that *Mycobacterium bovis* is absent from the domestic herd, but is instead awarded to a territory where both the incidence and prevalence of bTB amongst cattle herds has remained below 0.1% per year for 6 consecutive years and appropriate surveillance programs are in place to detect new herd breakdowns. Although Scotland has successfully maintained bTB incidence below 0.1%, new breakdowns continue to be identified through routine surveillance each year and, as with other OTF countries, the import of infected cattle from bTB endemic regions is believed to be the leading risk factor (Gilbert et al., 2005; Green and Cornell, 2005; van Asseldonk et al., 2005; Schiller et al., 2011)

Recognizing the importance of cattle movements in spreading bTB, the Scottish government introduced legislation in September 2005 that required all cattle imported from high incidence parishes of England and Wales to be tested for bTB within 60 to 120 days of arriving in Scotland at the receiving farmer's expense. Surveys have estimated the direct veterinary costs of testing range from £5.50 to £9.00 per animal, although the actual costs may be higher due to labour expenses, disruptions in farm business practices, and missed marketing opportunities (Anonymous, 2006; Bennett, 2009). The legislation includes exceptions for cattle that were subject to *post-mortem* examination for lesions consistent with bTB at slaughterhouses within 120 days of arrival and for cattle that were subject to *ante-mortem* testing as part of a routinely scheduled herd test in the receiving herd within 120 days of arrival. Similar post-movement testing of cattle imported from Northern

Ireland and the Republic of Ireland was required throughout the time period leading up to OTF recognition.

The main objective of post-movement testing was to ensure that infected cattle were quickly identified and removed before disease could spread to other Scottish animals or herds. However, any legislation that imposes financial or logistical barriers to cattle trade also has the potential to change farmer behaviour and movement patterns (Vernon and Keeling, 2012). For example, when complementary pre-movement testing was introduced in May 2006 for all cattle over 6 weeks of age moving off farms in high incidence parishes of England and Wales, Christley and colleagues (2011) found evidence that farmers in these regions reduced the size and frequency of cattle batch movements to minimize testing costs. These indirect deterrent effects on cattle import trade may have an equally important role in limiting the opportunities for bTB to be introduced into Scotland and subsequently the risk of detecting new breakdowns through routine herd surveillance.

In this analysis, longitudinal surveillance data and movement records was used to investigate the influence of post-movement testing legislation on import patterns and associated risks for bTB breakdowns in Scotland from 2002 to 2009. First, the frequency and demographic characteristics of individual cattle imported into Scotland in the 4 year periods immediately before (2002 to 2005) and after (2006 to 2009) the introduction of post-movement testing legislation were compared to identify changes in the types of cattle farmers are willing to import. Next, changes in farm-level import patterns between the two study time periods were quantified to document the deterrent effects of testing legislation on cattle import trade. Finally, logistic regression analyses were used to determine whether the farm-level risk of being identified as a breakdown through routine testing or slaughter surveillance and the animal-level risk of being identified as a reactor in a breakdown herd associated with import movement history have also correspondingly changed

between time periods through the direct and indirect protective effects of movement testing legislation.

Methods

Routine surveillance for bTB in Scotland

In the period leading up to OTF recognition in Scotland, routine surveillance for bTB in cattle was conducted using three methods: (1) *post-mortem* examination of all bovine carcasses at abattoirs for visible pathognomonic lesions of bTB, (2) routine herd tests (RHT) to monitor the infection status of individual herds, and (3) targeted post-movement testing of cattle imported from regions with high bTB incidence. A RHT is normally conducted once every 4 years and includes all female cattle that have previously calved, bulls greater than 12 months old unless exempted by a veterinarian, any cattle greater than 6 weeks old which could be used for breeding, and any cattle purchased since the last RHT. A small number of herds considered to be at increased risk of acquiring and transmitting bTB, including those with regular intake of cattle from the Republic of Ireland or Northern Ireland and those that retail raw milk, are subject to a greater frequency and intensity of testing.

The single intradermal comparative cervical tuberculin sensitivity test (SICCT) used for both RHT and movement-associated testing compares the sensitivity of individual cattle to bovine and avian mycobacterial antigens injected intradermally at separate sites on the neck. Depending on the relative degree of reaction to the antigens after 72 hours and the perceived herd-level risk for bTB, animals may be classified as positive reactors, inconclusive reactors, or negatives (Green and Cornell, 2005). The sensitivity of SICCT for detecting infected cattle ranges from 68% to 99% and the specificity ranges from 79% to 99% (de la Rua-Domenech et al., 2006; Clegg et al., 2011). For that reason, a new bTB herd breakdown is only considered "confirmed" if either visible pathognomonic lesions of infection with *M. bovis* are observed during *post-mortem* examination of positive

reactors or *M. bovis* is cultured from tissue samples. Cattle with an inconclusive SICCT may be re-tested up to two times or slaughtered to examine for visible lesions. The sensitivity of *post-mortem* examination for identifying cattle with visible lesions ranges from 86% to 95% (Byrne, 1992; Corner, 1994; Whipple et al., 1996; Norby et al., 2004).

Results of all *ante-mortem* bTB tests in Great Britain and information on suspected and confirmed cases identified through slaughter surveillance have been collated in the VETNET database maintained by the Department for Environment, Food and Rural Affairs (DEFRA) since the 1990s. Negative RHT results for a herd are reported *en masse* with the following summary information: number of cattle tested, total number of animals in the herd, date and type of test, herd production type, and administrative information for the farm including its unique county-parish-holding (CPH) identifier. When a positive or inconclusive reactor is identified, the passport number of the animal is entered along with any follow-up test results or actions taken. For herds with multiple reactors, the information on whether lesions were observed at *post-mortem* examination or positive cultures for *M. bovis* were obtained from tissue samples is aggregated at the herd level.

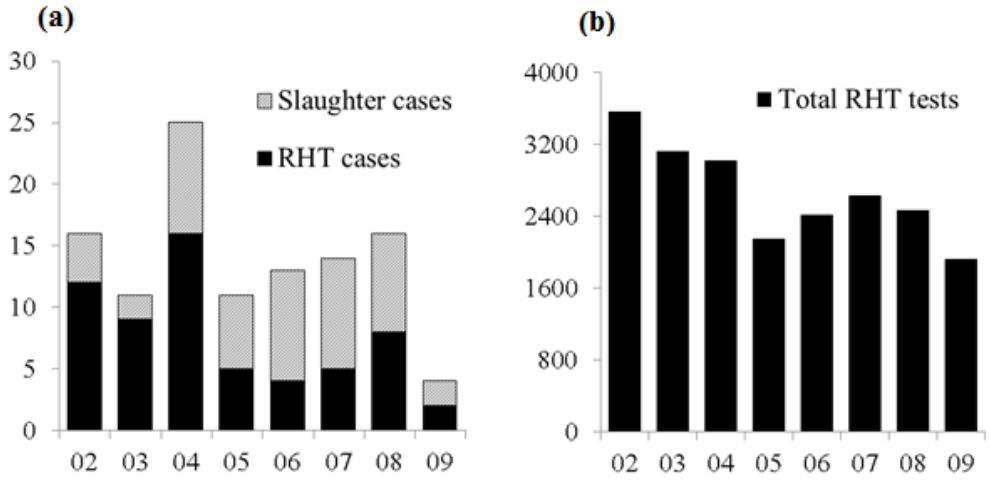
Criteria for selection of cases

Extracts of the VETNET database relevant to Scotland from 2002 to 2009 were received from the Information Management Team of Animal Health. Following the formal definition of a new herd breakdown used throughout Great Britain during the study years, an RHT case was defined as any cattle herd where at least one SICCT positive reactor was identified on a RHT, and infection was subsequently confirmed through observation of lesions at *post-mortem* examination or isolation of *M. bovis* from tissue samples of the reactors. A slaughter case was defined as any cattle herd with at least one animal identified with visible bTB lesions at slaughter that triggered an entry in the VETNET database. For herds where confirmed positive reactors at routine testing or cattle with visible lesions at

slaughter were identified on more than one occasion from 2002 to 2009, only the first observation of a bTB infected animal was analysed as the case. Other breakdown types, including breakdowns identified through contact tracing tests, new or re-formed herd tests, and post-movement tests, were not considered as these were directly attributable to animal movements from other breakdown herds.

There was a total of 63 cases (42 RHT and 21 slaughter) from 01 January 2002 to 31 December 2005, corresponding to the 4-year period before introduction of pre- and post-movement testing legislation, and a total of 47 cases (19 RHT and 28 slaughter) from 01 Jan 2006 to 31 Dec 2009, corresponding to the 4-year period after introduction of pre- and post-movement testing legislation. The distribution of cases and the number of herds subject to RHT by year are shown in Figure 9.1. Comparisons between the two 4-year time periods were used to understand how legislation influenced cattle import movements into Scotland and the risk of experiencing a new herd breakdown identified through routine herd surveillance.

Figure 9.1: (a) Distribution of bTB breakdowns detected through slaughter and RHT in Scotland and (b) total number of herds in Scotland subject to RHT by year from 2002 to 2009.



Criteria for characterizing import movements

Information on the movement history and demographic profiles of individual cattle and farms was extracted from the Cattle Tracing System (CTS) database operated by the British Cattle Movement Service (BCMS). Cattle keepers have been required to report all births, deaths, and movements of individual animals centrally to BCMS since January 2001, although limited information on earlier movements is available from efforts to back-capture information for animals that were alive, but not yet registered in the system as of 2001. CTS data quality has improved markedly since 2002 (Green and Kao, 2007). The April 2010 CTS extract containing all cattle movement records up to that date was provided by the Rapid Analysis and Detection of Animal-related Risks (RADAR) project as a series of nine data tables with accompanying reference keys.

For the purpose of this analysis, the term 'farm' refers to a location identified as an agricultural holding or a landless animal keeper (a farmer who raises cattle on rented land) in the CTS database. From 2002 to 2009, there were a total of 16,716 farms in Scotland that had a valid CPH code and at least one cattle movement record. Of these, 10,683 farms had cattle present in both January 2002 and January 2009, based on summary statistics in the Animal Population data table, indicating continuity of cattle farming through the entire study period.

The unique CTS livestock identifiers of all animals imported into Scotland from 01 January 2002 to 31 December 2005 and from 01January 2006 to 31 December 2009 were extracted from the Livestock Movements data table. This included animals that moved directly between farms and animals that were imported through sales at livestock markets. Temporary cross-border movements to markets and rare movements to and from other location types outside Scotland, such as showgrounds, artificial insemination centres or calf collection centres, and movements to abattoirs were excluded. If an animal was imported to Scotland and subsequently moved to another farm within the same study time period, both farms were considered to have received imported cattle during the study time period.

However, post-import movements that occurred across study time periods were not considered to ensure that farms in the 2006 to 2009 study period were subject to the same left-censoring bias as farms in the 2002 to 2005 study period. Although the number of such movements was small, their exclusion may lead to underestimation of the farm-level risk of acquiring bTB through cattle import movements.

The frequency of RHT in cattle herds within a given parish of Great Britain ranges from 1 to 4 years based on the incidence of recent breakdowns and the perceived risk of local bTB transmission between herds. Farms in high incidence parishes are tested annually. Buffer zones with 2 or 3 year testing interval may be created around these regions to increase the probability of detecting new spread. A high incidence region of England or Wales was therefore classified as one where the parish testing interval (PTI) was 1 or 2 years and a low incidence region of England or Wales was classified as one where the PTI was 3 or 4 years based on the list of PTIs published by DEFRA in 2007. Parishes of Scotland were treated as a separate category from low-incidence regions of England and Wales because of Scotland's OTF status. Parishes of Ireland, Northern Ireland, and other overseas countries were grouped together under overseas imports. This was done to classify the origins of cattle imported into Scotland, and determine if any of the farms where cattle were located prior to import were in regions with high bTB incidence.

Analysis of changes in import animal demographics

The purpose of this analysis was to establish whether farmers changed their behaviour by importing different types of cattle or shifting the timing of movements to avoid the additional costs imposed by movement-associated bTB testing. Since the regulatory changes applied only to cattle imported from high incidence parishes of England and Wales, the observed trends in imports from low incidence parishes were used to distinguish the effects of legislative change from other demographic processes acting simultaneously on the Scottish cattle industry. Comparisons were

also made to imports from overseas, although the frequency of movements was disproportionately low compared with imports from Great Britain.

For each imported animal, records of all known locations prior to import and all locations in Scotland following import were extracted from the CTS Livestock Locations data table. The total number of days each imported animal spent in parishes of England and Wales with testing intervals of 1, 2, 3 or 4 years prior to import were calculated based on the start date and end date at the location extracted from the CTS Livestock Locations data table. Animals were then assigned into risk categories based on their location history: (i) animals imported from low incidence parishes, (ii) animals imported from high incidence parishes, and (iii) animals imported directly to Scotland from overseas. It should be noted that 13.8% of animals in the high incidence category also had recorded movements through low incidence parishes prior to import.

The CTS Livestock identifier of each imported animal was then linked to the CTS Livestock data table to generate the following demographic variables: sex, breed classification (dairy, beef, or dual purpose breed), date of import into Scotland, and the age at time of import. The date of birth was missing for 1,232 of the 280,511 cattle imported from 2002 to 2005 and for 161 of the 177,632 cattle imported from 2006 to 2009. The CTS Livestock Relationships data table was used to create a binary variable indicating whether female cattle imported from England and Wales calved prior to moving into Scotland. For the small subset of animals that were exported and then re-imported within the 4-year time period, only the first import date was selected to record the demographic characteristics.

For animals that were slaughtered as of April 2010, the time from import to slaughter in Scotland was calculated and used to create a binary variable "slaughtered within 120 days of import". For animals that were present on a Scottish farm when a RHT test was conducted after import, the earliest time from import to RHT was calculated and used to create a binary variable "subject to RHT within 120 days of import" to coincide with post-movement testing regulations

requiring that imported animals to be tested for bTB within 120 days of import unless sent to slaughter. The 2006 to 2009 time period was right-censored by the available CTS and VETNET data and because of that, for the analysis of animals subject to slaughter within 120 days, only imports from 01 Jan 2006 to 01 Nov 2009 were considered and for the analysis of animals subject to RHT within 120 days, only imports from 01 Jan 2006 to 01 Sept 2009 were considered. Odds ratios with 95% confidence intervals were calculated for the binary variables slaughtered within 120 days, subject to RHT within 120 days, and calved prior to import to establish whether testing legislation influenced the frequency or types of cattle imported.

Analysis of changes in national and farm level import patterns

The animal-level import data were then aggregated at the farm-level and national-level to characterize changes in the intensity of exposure to imported cattle between the two 4-year time periods. For each Scottish farm, the total number of cow-days from January 2002 through December 2005 and from January 2006 through December 2009 was extracted from the CTS Animal Population data table. The proportions of total cow-days belonging to animals imported from low incidence parishes, animals imported from high incidence parishes, and animals imported directly to Scotland from overseas were calculated as a combined measure of the number of cattle imported and the duration of stay following import.

Within each of the 4-year time periods, individual farms were assigned into five risk categories based on the origin of cattle imported: (i) farms with movements from Scotland only, (ii) farms with animals from low incidence parishes of England and Wales, (iii) farms with animals from high incidence parishes of England and Wales, (iv) farms with animals imported from overseas, and (v) farms with animals both from high incidence parishes and animals from overseas. Although some of the farms in the latter three categories also had movements from low incidence parishes, the primary risk of bTB introduction was assumed to be from animals imported from high incidence parishes or overseas.

Descriptive statistics of changes in farm risk classification in 2006 to 2009 compared to 2002 to 2005 for the subset of 10,683 farms that continuously farmed cattle from 2002 to 2009 were obtained. A z-test was used to evaluate statistical significance of the change in the proportion of farms with imports from high incidence parishes (categories (iii) and (v) combined) in 2002 to 2005 compared with 2006 to 2009. For the 1,668 farms that imported cattle from high incidence regions in both 4-year periods, Wilcoxon signed rank test was used to evaluate statistical significance of the changes in the total number of cattle imported from high incidence regions, the average number of days spent on the farm following import, and the proportion of total cow-days within each time period contributed by animals imported from high incidence regions.

Analysis of changes in the animal-level risks of being identified as a reactor in a breakdown herd

The primary objective of introducing post-movement testing was to provide an opportunity to detect infected cattle faster than RHT or slaughter surveillance thereby limiting the potential further transmission within Scotland. In this analysis, the risks for an imported animal for being identified as a positive reactor in a breakdown herd were compared between the two 4-year time periods to establish whether regulatory changes influenced the likelihood of infected imports being detected through routine surveillance. A case was defined as an animal identified as a positive reactor on the initial RHT or herd-test triggered by slaughter detection, and any follow-up testing in the herd during the breakdown. A control was any other animal present on the farm at the time according to the CTS Livestock Locations data table, including animals with negative SICCT results, inconclusive reactors, and dangerous contacts.

A total of 1,074 individual cattle were flagged in VETNET as reactors on either the initial breakdown herd-test or the follow-up tests in the 103 breakdown herds where the CPH number could be linked to the CTS database; 261 cattle in the

period from 2002 to 2005 and 813 cattle in the period from 2006 to 2009. To ensure that both time periods were subject to the same right-censoring, records for 14 of the 261 reactors from breakdown herds in 2002 to 2005 that were identified on follow-up tests occurring in 2006 to 2009 were discarded. Because the follow-up results are aggregated at the herd level in VETNET, it was not possible to determine which of the individual reactors were confirmed by isolation of *M. bovis* or visible lesions at *post-mortem* examination. All positive reactors in the confirmed breakdown herds were therefore considered to be confirmed.

The ear tag number for 944 of the reactors matched with an ear tag number from the list of 36,647 cattle present in the breakdown herds +/- 7 days from when the first reactor was identified during the breakdown. The assumption was made that all cattle present in the herd were tested for bTB as part of standard breakdown eradication procedures. All known movement history prior to the breakdown date for each of the 36,647 animals was extracted from the CTS Livestock Locations data table, including records of movements that occurred prior to 2001. Animals were then assigned into risk categories based on their location history breakdown date: (i) animals located exclusively in Scotland, (ii) animals imported from low incidence parishes, (iii) animals imported from high incidence parishes, and (iv) animals imported directly to Scotland from overseas. A univariate logistic regression analysis was performed within each 4-year time period to evaluate the odds for an animal to be identified as a reactor based on the movement risk category. Herd was included as a random effect in the model to account for variation in the number of cattle and reactors present on the breakdown date.

Analysis of changes in the farm-level risk of being identified as a breakdown herd

Some delay between the introduction of control measures and changes in disease incidence is to be expected in bTB eradication programs (Gordejo and Verneersch, 2006) and this analysis investigated whether pre- and post-movement

testing reduced the herd-level risk of breakdowns associated with cattle import movements. A case was defined as a herd that continuously farmed cattle from 2002 to 2009, and experienced a confirmed bTB breakdown identified through RHT or slaughter surveillance in the corresponding 4-year period. A further 7 herds were excluded because the CPH number recorded in the VETNET database could not be linked to a valid CTS location identifier leaving a total of 56 cases from 2002 to 2005 and 41 cases from 2006 to 2009. The control groups was comprised of the 9,730 farms that continuously housed cattle from 2002 to 2009 and had at least one bTB test observation recorded in the VETNET database within each 4-year time period.

A univariate logistic regression analysis was performed for each 4-year period to evaluate the odds of being a breakdown herd based on the five previously described movement-based risk categories. To further explore changes in risk associated with imports from high incidence parishes, farms with imports from high incidence parishes of England and Wales (category iii) and farms with imports from both high incidence parishes and overseas (category v) were aggregated into a single category. Within each 4-year period, the subset of farms with animals from high incidence parishes was compared to the subset of farms with animals from low incidence parishes of England and Wales to establish whether the risk of being a breakdown herd was greater for farms that imported animals from high incidence regions. Between the two time periods, the risks of being a breakdown herd in the subset of farms that imported animals from high incidence parishes were also compared. Both analyses assumed a one-tailed probability distribution to evaluate statistical significance.

Results

Changes in import volume and import animal demographics

The total number of cattle imported into Scotland decreased substantially between time periods with 177,632 cattle imported from 2006 to 2009 compared to 280,136 from 2002 to 2005. Proportionately fewer cattle were imported from high incidence parishes in England and Wales in 2006 to 2009 (27.1%) compared to 2002 to 2005 (46.2%) and there was an immediate reduction in the number of cattle imported from high incidence parishes of England and Wales following the introduction of post-movement testing legislation in September 2005 (Figure 9.2). No appreciable changes were observed in the number of cattle imported from overseas.

Figure 9.2: Frequency of import movements into Scotland from high incidence and low incidence parishes of England and Wales, and from overseas by year from 2002 to 2009. The asterisk (*) on the left indicates the date when post-movement testing legislation was introduced and the asterisk (*) on the right indicates the date when pre-movement testing legislation was introduced.

The median age at import increased by 116 days for cattle imported from high incidence parishes and by 63 days for cattle imported from low incidence

parishes in 2006 to 2009 compared to 2002 to 2005 (Table 9.1). For both high and low incidence regions, a greater proportion of imported cattle were female (65.3% versus 54.8%) and these animals had significantly greater odds of having at least one recorded calving prior to import than cows imported from 2002 to 2005 (OR: 1.92, 95% CI: 1.85 – 1.99, $p < 0.001$). However, similar changes were also observed for cattle imported from low incidence regions. There was no appreciable difference in the distribution of imports by breed classification within or between the two time periods.

In 2006 to 2009, the odds of being slaughtered within 120 days of import increased by a factor of 1.76 (95% CI: 1.71 – 1.80, $p < 0.001$) for cattle from high incidence parishes and by a factor of 1.48 (95%CI: 1.45 – 1.52, $p < 0.001$) for cattle from low incidence parishes compared to 2002 to 2005 (Table 9.1). Cattle from high-risk parishes in 2006 to 2009 had significantly greater odds of moving into a herd subject to RHT within 120 days of import (OR: 1.21, 95% CI: 1.15 – 1.28, $p < 0.001$) while the opposite was true for cattle imported from low-risk parishes (OR: 0.78, 95% CI: 0.75 – 0.81, $p < 0.001$). However, only a small fraction of imported cattle (<5%) in each time period were subject to such testing. Within each time period, the demographic characteristics of cattle from high incidence parishes were not appreciably different from the demographic characteristics of cattle from low incidence parishes, except for age at import.

Table 9.1: Changes in the demographic profile of animals imported into Scotland from high incidence (High) and low incidence (Low) parishes of England and Wales in 2006 to 2009 compared to 2002 to 2005. The 95% CIs are shown below the ORs.

Variable	Region	Values	2002 - 2005		2006 – 2009		Odds ratios
			N	%	N	%	
Total animals imported			280136	100	177632	100	-
		High	129408	46.2	48,210	27.1	-
		Low	128630	45.9	102659	57.8	
Age at import (days)	High	Mean	484		706		-
		Median	421		537		
		SD	492		789		
	Low	Mean	534		674		-
		Median	438		501		
		SD	563		742		
Sex	High	Male	58504	45.2	16697	34.6	-
		Female	70904	54.8	31513	65.3	
	Low	Male	58395	45.4	39966	38.9	-
		Female	70235	54.6	62693	61.1	
Breed classification	High	Beef	112815	87.9	41830	86.8	-
		Dairy	15553	12.0	5857	12.2	
		Dual	973	0.75	510	1.06	
	Low	Beef	107880	83.8	85092	82.9	-
		Dairy	20037	15.6	16171	15.8	
		Dual	618	0.48	1382	1.35	
Calved prior to import (female cattle only)	High	No	61831	87.9	24517	79.1	OR: 1.92 ***
		Yes	8497	12.1	6472	20.9	(1.85 - 1.99)
	Low	No	58174	82.8	49254	78.6	OR: 1.32 ***
		Yes	12061	17.2	13439	21.4	(1.28 – 1.35)
Slaughtered within 120 days †	High	No	110284	85.2	35827	77.4	OR: 1.76 ***
		Yes	19124	14.8	10916	22.6	(1.71 – 1.80)
	Low	No	104723	81.4	74438	75.4	OR: 1. 48 ***
		Yes	23907	18.6	25243	24.6	(1.45 – 1.52)
Subject to RHT within 120 days ‡	High	No	124834	96.5	42650	95.8	OR: 1.21 ***
		Yes	4574	3.5	1900	4.1	(1.15 – 1.28)
	Low	No	122307	95.1	91695	96.4	OR: 0.78 ***
		Yes	6323	4.9	3703	3.6	(0.75 – 0.81)

*** Indicates significance at $p < 0.001$ level

† For the 2006 to 2009 period, only cattle imported before 01 Nov 2009 were included

‡ For the 2006 to 2009 period, only cattle imported before 01 Sep 2009 were included

Changes in national and farm level import patterns

The overall intensity of exposure of Scottish cattle herd to imported cattle, measured as the proportion of total cow-days in Scotland contributed by imported animals, decreased from 3.56% in 2002 to 2005 to 2.12% in 2006 to 2009 (Table 9.2). Proportionately fewer cow-days in 2006 to 2009 were contributed by animals imported from high incidence parishes of England and Wales compared to 2002 to 2005.

Table 9.2: Changes between the periods 2002-2005 and 2006-2009 in the percentage of total cow-days in Scotland contributed by animals imported from high incidence parishes of England and Wales, low incidence parishes of England and Wales, and from overseas

	Low incidence	High incidence	Overseas import	Total
2002 to 2005				
Absolute % of total cow-days	1.59 %	1.63%	0.34%	3.56%
Relative % of import cow-days	44.7%	45.7%	9.6%	100%
2006 to 2009				
Absolute % of total cow-days	1.18%	0.60%	0.34%	2.12%
Relative % of import cow-days	55.7%	28.3%	16.0%	100%

In evaluating changes in the movement-based risk classification of the 10,683 farms that continuously housed cattle from 2002 to 2009, 60% of farms kept same risk classification and 19.3% of farms that imported cattle from high incidence parishes in 2002 to 2005 were no longer doing so in 2006 to 2009 (Table 9.3). The overall proportion of farms importing cattle from high incidence parishes significantly ($z = -26.2$, $p < 0.001$) decreased from 31.1% in 2002 to 2005 to 15.7% in 2006 to 2009.

Table 9.3: Changes in the movement-based farm risk classification between the periods 2002-2005 and 2006-2009 for the 10,683 Scottish farms that continuously housed cattle.

		Risk classification 2006 to 2009					
		Scotland only	**Low incidence parishes[1]**	**High incidence parishes[2]**	**Overseas imports**	**Both high incidence and overseas**	**Total**
Risk classification 2002 to 2005	**Scotland only**	4457 (41.7%)	460 (4.3%)	245 (2.2%)	82 (0.8%)	31 (0.3%)	**5275 (49.3%)**
	Low incidence parishes	706 (6.6%)	272 (2.5%)	188 (1.8%)	59 (0.6%)	32 (0.3%)	**1257 (11.7%)**
	High incidence parishes	1191 (11.1%)	700 (6.6%)	1055 (9.9%)	135 (1.3%)	241 (2.3%)	**3322 (31.1%)**
	Overseas imports	104 (1.0%)	53 (0.5%)	26 (0.2%)	32 (0.3%)	15 (0.1%)	**230 (2.2%)**
	Both high incidence and overseas	75 (0.7%)	94 (0.9%)	167 (1.6%)	58 (0.5%)	205 (1.9%)	**599 (5.6%)**
	Total	6533 (61.2%)	1579 (14.7%)	1681 (15.7%)	366 (3.4%)	584 (4.9%)	**10683 (100%)**

[1] Imports from low incidence parishes of England and Wales.
[2] Imports from high incidence parishes of England and Wales.

For the subset of 1,668 farms that imported cattle from high incidence parishes of England and Wales in both time periods, the average number of animals imported from high incidence parishes per farm and proportion of total cow-days on a farm contributed by animals from high incidence parishes were significantly lower in 2006 to 2009 than in 2002 to 2005 based on Wilcoxon signed-rank tests ($p < 0.001$) (Table 9.4). However, the average number of cow-days spent on the farm following import was not significantly different (481 days compared to 463 days, $p = 0.411$).

Table 9.4: Changes in the intensity of exposure to cattle imported from high incidence parishes of England and Wales in the subset of 1,668 Scottish farms with such imports in both the periods 2002-2005 and 2006-2009.

Variable	Period	Mean	Min	Median	Max	Wilcoxon signed-rank test
Number of imported animals	2002 to 2005 2006 to 2009	59.95 26.77	1 1	11 4	3424 2435	$p < 0.001$
Average number of cow-days following import	2002 to 2005 2006 to 2009	463.4 480.9	1 1	418.8 408.7	1451 1422	$p = 0.411$
Proportion of total cow-days contributed by imported animals	2002 to 2005 2006 to 2009	0.0471 0.0235	<0.001 <0.001	0.0159 0.0049	0.7441 0.7929	$p < 0.001$

Changes in animal-level risks of being identified as a reactor in a breakdown herd

There was evidence that the risks for an imported animal to be identified as a positive reactor in a breakdown herd decreased following the introduction of pre- and post-movement testing legislation (Table 9.5). From 2002 to 2005, animals that were imported from high incidence parishes of England and Wales prior to the initial breakdown date had3.53 times greater odds of being identified as reactors during the breakdown than Scottish animals (95% CI: 1.96 – 6.33, $p < 0.001$), and animals imported from overseas had 2.62 times greater odds of being identified as reactors (95% CI: 1.11 – 6.13, $p = 0.027$). In the period from 2006 to 2009, no single group of animals was at a significantly increased risk. However, imports constituted only approximately 20% of cattle identified as reactors in both the time periods; the other 80% were animals that were only ever located in Scotland. There was also marked heterogeneity in the number of positive reactors identified in a breakdown herd with a median of 4, a mean of 12.6, and a maximum of 134.

Table 9.5: Changes in the animal-level risk of being identified as a reactor in a bTB breakdown herd in Scotland identified through routine surveillance between the periods 2002-2005 and 2006-2009 based on import movement history.

	N	Cases	Controls	OR	95% CI	p-value
2002 to 2005						
Scotland only	18,390	171	18,219	1.00	-	-
Low incidence parish	717	16	701	1.80	0.94 – 3.47	0.076
High incidence parish	771	21	750	3.53	1.96 – 6.33	< 0.001
Overseas import	662	10	652	2.62	1.11 – 6.13	0.027
2006 to 2009						
Scotland only	14,479	628	13,851	1.00	-	-
Low incidence parish	629	60	569	1.28	0.89 – 1.86	0.184
High incidence parish	392	32	360	1.15	0.76 – 1.76	0.507
Overseas import	483	6	477	1.39	0.35 – 2.48	0.887

Changes in the farm-level risks of being identified as a breakdown herd

At the herd level, import movements were important in determining the risk of being identified as a breakdown herd through routine surveillance during both time periods (Table 9.6). Farms that imported animals from high incidence parishes of England and Wales in 2002 to 2005 had3.81 times greater odds of experiencing a breakdown than farms with no import movements (95% CI: 1.83 – 8.54, $p < 0.001$). From 2006 to 2009, herds with import movements from high incidence parishes were still at increased risk (OR: 2.59, 95% CI: 1.03 – 6.27, $p = 0.025$). However, importing animals from both high incidence parishes and overseas carried no greater risk than importing animals from either region alone. In both time periods, farms that imported animals from low incidence parishes were at no greater risk than farms without import movements (Table 9.6).

Table 9.6: Changes in the farm-level risks for being identified as a breakdown herd through routine surveillance in Scotland associated with importing cattle from high incidence parishes of England and Wales, low incidence parishes of England and Wales, and from overseas in 2006 to 2009 compared to 2002 to 2005.

	N	Cases	Controls	OR	95% CI	p-value
2002 to 2005						
Scotland only	4737	11	4726	Ref	-	-
Low incidence parish	1177	4	1173	1.46	0.33 – 4.96	0.517
High incidence parish	3064	27	3037	3.81	1.83 – 8.54	< 0.001
Overseas import	223	6	217	11.9	3.57 – 35.4	< 0.001
Both high incidence and overseas imports	585	8	577	5.95	2.06 – 16.3	< 0.001
2006 to 2009						
Scotland only	5825	14	5811	Ref	-	-
Low incidence parish	1474	6	1468	1.69	0.53 – 4.71	0.268
High incidence parish	1614	10	1604	2.59	1.03 – 6.27	0.025
Overseas import	346	4	342	4.85	1.15 – 15.6	0.018
Both high incidence and overseas imports	512	7	505	5.75	1.95 – 15.3	0.001

Combining data from categories (iii) and (v) into a single category representing all farms with imports from high incidence parishes of England and Wales, farms that imported cattle from high incidence parishes between 2002 and 2005 had significantly greaer odds of being identified as breakdown herds than farms that imported cattle from low incidence parishes in the same time period (OR: 2.83, 95% CI: 1.15 – 8.76, p = 0.039). However, between 2006 and 2009, farms that imported cattle from high incidence parishes were at no greater odds of being identified as breakdown herds than farms that imported cattle from low incidence parishes (OR: 1.97, 95% CI: 0.85 – 5.10, p = 0.201). Furthermore, farms that imported cattle from high incidence parishes in 2006 to 2009 were noat no greater odds of beingidentified as breakdown herds than farms that imported cattle from high incidence parishes in 2002 to 2005 (OR: 0.83, 95% CI: 0.48 – 1.40, p = 0.57).

Discussion

Monitoring changes in risk factors over the course of a disease eradication program is important for establishing program efficacy and informing future policy decisions (Bicknell et al., 1999; Gramig and Horag, 2011). In this analysis, there was evidence that although the relative and absolute frequency of cattle imports from parishes of England and Wales with high bTB incidence has changed substantially since the introduction of pre- and post- movement testing legislation, the movement-based risk factors associated with new herd breakdowns in Scotland have yet to appreciably change. Farms with a recent history of importing cattle from high incidence parishes and from overseas countries are still significantly more likely to experience bTB breakdowns identified through routine surveillance than farms with no recent import movements. While some delay between the introduction of control measures and changes in disease incidence is to be expected in bTB eradication programs (Gordejo and Verneersch, 2006), other study findings point to several unique features of bTB epidemiology in Scotland that may be influencing transmission dynamics.

Changes in import patterns

There is growing awareness in both the veterinary and public health fields that behavioural feedback can influence the success of disease eradication programs (Robinson et al., 2007; Risau-Gusman and Zanette, 2009; Funk et al., 2010; Meloni et al., 2011). Similar to findings from Christley and colleagues (Christley et al., 2011), there was evidence that farmers modified their trading patterns in response to pre- and-post movement testing requirements. More than 80% of the overall decline in cattle imports in 2006 to 2009 compared with 2002 to2005 was attributed to decreased movements from high incidence parishes of England and Wales. There was also a small, but significant increase in the likelihood of animals imported from high incidence parishes being slaughtered or tested through RHT within the 120 day limit for post-movement testing following arrival in Scotland. This may reflect

differences in the types of cattle that farmers from high incidence parishes are willing to sell and/or the types of cattle for which farmers in Scotland are willing to incur additional costs and risks to buy. Irrespective of origin, a greater proportion of animals imported after 2006 were female animals with at least one recorded calving suggesting there may be a relative increase in market demand for replacement breeding cattle. This has important implications for risks of bTB transmission as older cows are significantly more likely to be identified as reactors in breakdown herds (Griffin et al., 1996; Ramírez-Villaescusa et al., 2008) and bTB infected dams tested within the first four to six weeks post-calving are significantly less likely to react to SICCT (Monaghan et al., 1994). Recent import movements may therefore carry higher risk of bTB introductions due to changes in animal demographics, despite the perceived efficacy of pre- and post-movement testing.

If testing costs were the only motivating factor behind changes in import animal demographics, there should have more marked differences between animals imported from high incidence parishes compared to low incidence parishes, which were not subject to the same testing requirements during the years of study. Instead, apart from age at import, the demographic profiles were virtually identical. Without accurate data on animal movements prior to 2001, it is difficult to separate the effects of the 2001 foot-and-mouth disease (FMD) epidemic from the effects of pre- and post-movement testing legislation on the observed changes in import movement patterns. Post-FMD in 2002, there was a transient increase in between-herd cattle movements as farmers purchased cattle to restock culled herds. Changes in the type and number of cattle imported to Scotland over time may simply reflect a return to baseline trading patterns. Pre-movement and post-movement testing legislation was expanded in February 2010 to include all animals imported from England and Wales regardless of their origin, highlighting the continued need for monitoring the behavioural changes and risks associated with all types of cattle imports.

Changes in movement-based risks for imported animals and receiving farms

Longitudinal databases such as VETNET and CTS provide the unique opportunity to study the rate and scale at which behavioural change and disease specific interventions influence transmission risk over the course of an eradication program. The change in industry wide import patterns reducing the intensity of exposure to high-risk animals was seen almost immediately following the introduction of bTB pre- and post-movement testing legislation. However, there was an observable delay in the subsequent reduction of farm-level risks of a breakdown associated with cattle imports. At the animal level, it was found that from 2002 to 2005 animals imported from high incidence parishes of England and Wales or from overseas were significantly more likely to be identified as reactors in breakdown herds identified through routine surveillance in Scotland, while from 2006 to 2009 no single group of animals was at increased risk. One possible explanation is that the definition of a new herd breakdown used in this study excluded those that were triggered directly by post-movement tests, which were considered to be part of the change in prevention practices. Routine herd testing and slaughter surveillance likely played a greater role in identifying infected imports prior to 2006. It is also likely that complementary pre-movement testing on the farms of origin in England and Wales has been effective in reducing the number of infected cattle entering Scotland.

The changes in individual animal-level risk have yet to translate into a reduction in overall farm-level risk for bTB breakdowns associated with cattle imports. In both the periods 2002 to 2005 and 2006 to 2009, farms with recent imports from high incidence parishes were significantly more likely to experience breakdowns and there was no significant difference in the magnitude of the odds ratios between the two periods. This reflects one limitation of the present study, which was the use of recent movement behaviour to estimate farm-level risk of exposure to cattle from high incidence parishes of England and Wales. Given the

relative infrequency of routine herd tests and the insidious nature of clinical signs, it is likely that many of the bTB breakdowns detected in Scotland from 2006 to 2009 were seeded before the legislative change and more time is needed to detect the resulting effect on farm-level risk. Re-stocking during the post-FMD recovery period is believed to have played an important role in increasing the incidence of new bTB breakdowns (Carrique-Mas et al., 2008). Fischer and colleagues (2005) report on an outbreak in the Netherlands observed by Paaijmans (Paaijmans, 2002) where the import of an infected animal generated a single additional case that was detected 392 days later. Another study from New Zealand documented eight cases arising in a dairy herd as the result of a single infected animal introduced over two years prior to detection (Barlow et al., 1997). This may also explain why more than 30% of breakdowns in each of the two periods could not be linked to recent imports from high-risk regions.

In practice, tracing of bTB infections is complicated not only by unknowns in biology of the disease and but also by mobility of cattle. Evidence from endemic regions of England and Wales shows that purchased cattle are overall at increased risk of being identified as reactors compared to homebred animals regardless of previous exposure history (Ramírez-Villaescusa et al., 2008). The process of transportation itself may provide opportunities for close contact to facilitate cattle to cattle transmission of bTB (Neill et al., 1989; Menzies and Neill, 2000; Goodchild and Clifton-Hadley, 2001). Efforts to trace the infection are complicated by possibility of multiple movements in animal lifetime. For example in the current study, at least 30% of the reactors in breakdowns herds were located on one or more other farms where bTB transmission may have taken place prior to joining the breakdown herd. In the period from 2002 to 2009, only a small fraction of new breakdowns in Scotland were identified through contact tracing.

Post-movement testing for overseas imports was required throughout the study time period and yet there was also no appreciable decline in the risk of the receiving farms experiencing breakdowns identified through routine surveillance.

Consistency in the number of foreign imports over time suggests that the additional costs and logistical constraints associated with testing have not deterred farms from purchasing cattle from overseas. From 2002 to 2009, a total of 13 herd breakdowns that were triggered by positive post-import tests of cattle imported from Northern Ireland or the Republic of Ireland were identified and excluded. The sensitivity of the bTB skin tests is not absolute and it is possible that infected cattle are escaping detection (de la Rua-Domenech et al., 2006). Further investigation into whether these animals were capable of transmitting bTB to the Scottish herd mates before detection would be beneficial for determining efficacy of current 120-day restrictions for post-movement testing in preventing disease introductions.

Potential for on-farm transmission

Given that approximately 80% of the reactors identified in breakdown herds were animals with no known history of movements outside Scotland, there is evidence to suggest that on-farm transmission may be contributing to the delay in reduction of farm-level risks. Heterogeneity in the number of positive reactors identified in a breakdown herd suggests that management practices have a strong influence on within-herd transmission dynamics (Olea-Popelka et al., 2008) and therefore on the risk of subsequently spreading bTB through cattle movements. A retrospective study of breakdown herds in Ireland found that cattle sold from herds with multiple reactors were significantly more likely to become positive on future tests than cattle from uninfected herds or herds with few infected animals (Wolfe et al., 2009).

Limitations of study findings

Neither the VETNET database nor the CTS database was originally designed to support epidemiological research and there were several limitations that may have influenced study findings. There were over 850 locations with cattle in the CTS database that had no routine herd test records and many CPHs with herd-test results in the VETNET database that had no cattle according to the CTS Livestock

Locations data table. Routine herd test results are stored in the VETNET database under the main farm CPH-identifier regardless of whether cattle are housed on that location or on other land parcels operated by the same cattle business (Madders, 2006). In many cases, farmers are not required to report movements between these 'linked' holdings, which may have led to underestimation of import movements or exposure to imported cattle. This also made it difficult to confirm that all cattle present on the CPH land parcel were tested as part of routine eradication procedures as was assumed in the animal-level risk factor analysis. Although the quality of CTS data has improved substantially over time, clerical errors or failure to report movements may have led to underestimation of the farm-level risk of introducing bTB through cattle imports (Green and Kao, 2007; Vernon, 2011).

Several additional factors made it difficult to accurately determine the disease status of individual animals present in breakdown herds and the risks associated with their past movement history. The method for recording *post-mortem* and culture results in the VETNET database meant that it was not possible to distinguish between confirmed and unconfirmed reactors in the study sample. The inclusion of false negative cattle is of particular concern because of potential biases in how results of SICCT are interpreted by individual veterinarians (Green and Cornell, 2005). If more severe interpretation criteria were applied to cattle imported from high regions, the logistic regression model may have overestimated the importance of movements in determining bTB risk. The γ -interferon (γ-IFN) assay, which can identify infected cattle earlier in the clinical progression of the disease and so provides a more objective assessment of disease status (Pollock et al., 2005), was introduced at the same time as post-movement testing legislation in 2005. This may partly explain the increase in the number of reactors identified in breakdown herds in 2006 to 2009 compared to 2002 to 2005. There were also a significant number of inconclusive reactors in breakdown herds that were assumed to be false positives, but had the potential to be infected with bTB. Given these limitations, the magnitude of the changes observed in animal-level risk analysis must be interpreted

with some caution. However, the general finding that on-farm transmission is contributing to bTB epidemiology should still be robust.

The method of classifying individual cattle and farms into movement risk categories was simply based on the presence or absence of import movements during each of the 4-year time periods. Other factors such as the number of cattle imported by the farm, the length of time animals spent in high-risk regions and the length of time they spent in Scottish herds following import are also likely important determinants of the risk for bTB introductions. However, these were not included in the present study because of issues with changes in CTS data quality over the years of study and difficulties in weighting the contribution of the more detailed import characteristics to overall risk (Mitchell et al., 2005; Green and Kao, 2007). The farm-level risk analysis may have been further confounded by demographic factors linked to both the likelihood of importing bTB through cattle movements and the likelihood of being detected as a breakdown herd through routine surveillance. Larger herds tend to purchase more cattle and other management factors such as higher stocking density and heavier environmental contamination may contribute to an increased frequency of on-farm transmission events (Griffin et al., 1996; White and Benhin, 2004; Green and Cornell, 2005; Reilly and Courtenay, 2007; Carrique-Mas et al., 2008; Brooks-Pollock and Keeling, 2009). The protocol for selecting animals for routine herd testing also means that a greater number of animals are tested in larger herds, which implicitly increases the odds of detecting both true positive and false positive reactors (Green and Cornell, 2005).

Conclusion

Although the incidence of bTB in Scotland has remained below the 0.1% required for OTF status, the appearance of new herd breakdowns each year highlights the need for continued vigilance and control. The deterrent effects of pre- and post-movement testing legislation on cattle imports from high incidence

parishes of England and Wales have no doubt changed the intensity of exposure to infected cattle, but the delay in reduction of farm-level risks suggests other factors may be influencing bTB epidemiology. For example, the analyses identified a potential role for cattle infected on Scottish farms to spread bTB prior to detection. With past movement history likely contributing to the current risk of herd breakdowns, more time may be needed to establish the strengths and weaknesses of using pre- and post-movement testing in bTB control. The study findings also emphasize the importance of considering how farmer behavioural change in response to disease interventions targeted at specific pathogens may influence the transmission dynamics of other diseases spreading through the same movement network.

Chapter 10

General discussion

Introduction

The main objective of this thesis was to provide empirical examples of why endemic diseases are challenging to control in cattle production systems and how insights gained from the analysis of national cattle movement records can be used to develop more effective disease control programmes in the future. One of the major recurring themes throughout the data chapters was that decisions made by individual famers can have profound effects on disease transmission dynamics at the industry level. In particular, there was evidence that modifying individual farm management practices to reduce the number of cattle movements and introducing trade restrictions to alter key epidemiological properties of the contact network were both potentially highly effective means of controlling multiple endemic diseases simultaneously. However, there are still many limitations in the current approaches to modelling endemic disease transmission that will require further refinement before the outputs can be used to inform national animal policy. The following sections discuss the implications of the main thesis findings for future investigations.

Control implications

From an epidemiological perspective, the most effective means of preventing endemic disease transmission in the cattle industry is still for farmers to maintain completely closed herds. This is, of course, impossible from a practical perspective, which has led virtually every published veterinary resource to recommend that all purchased cattle either be sourced from certified disease-free herds or quarantined and tested after purchase to reduce transmission risk. Findings from this thesis have provided additional evidence that these measures are infrequently adopted in practice and that a blanket approach to diagnostic testing is not necessarily the most

efficient use of disease control resources. As an alternative, it was shown that modifying individual farm management practices to reduce the number of cattle movements (a 'bottom up' approach) and introducing trade restrictions to alter key epidemiological properties of the contact network (a 'top down' approach) have significant potential to control multiple endemic diseases simultaneously. However, there are still significant gaps in our knowledge of these complex systems. In particular, there is a strong need for further research into the behavioural drivers of cattle movement patterns as well as the impact of other transmission mechanisms on the industry-level dynamics of endemic cattle diseases.

Diagnostic testing and surveillance

As highlighted by the comparison of performance indicators between BVDV seropositive and seronegative herds in Chapter 5, the clinical effects of endemic disease outbreaks are often highly variable and difficult for farmers to recognize under field conditions. This presents two major barriers to disease control. The first is that farmers may not be aware that disease is present in their herd and are therefore at risk of unknowingly spreading disease to farms in subsequent contact. The second is that farmers may not perceive the benefit to eradicating disease from their herd if it has no demonstrable impact on herd performance. Billinis and colleagues (2005) noted, for example, that dairy farmers in Greece were more likely to participate in a voluntary BVDV eradication programme if their herd had experienced significant reproductive losses. It has similarly been reported in Australia that herds participating in a voluntary Johne's disease control programmes were more likely to follow the recommended biosecurity measures when disease has been previously identified on the farm (Wraight et al., 2000). These findings emphasize the importance of conducting routine surveillance to identify infected herds as well as the importance of providing incentives for farmers to take appropriate controls in the event of a disease outbreak.

Compliance issues aside, the lack of affordable and accurate diagnostic tests remains one of the major barriers to eradicating endemic cattle diseases such as bovine tuberculosis (Schiller et al., 2011) and Johne's disease (Bastida and Juste,

2011). In Chapter 3 and Chapter 9, there was evidence that purchasing cattle from overseas countries with endemic bTB was a significant risk factor for herd breakdowns despite the fact that these imported animals were all subject to post-movement testing. There was also evidence from the BVDV survey data that relatively few beef cattle farms routinely performed diagnostic testing on purchased cattle and those that did were no less likely to be seropositive for BVDV. These findings stress that diagnostic tests reduce, but do not eliminate, the risk of disease spreading between herds through cattle movements.

The results from Chapter 3 also highlight a key challenge in conducting surveillance for endemic disease in low incidence regions using imperfect diagnostic tests: as the prevalence of disease declines, so does the predictive value of animal-level and herd-level test results (Martin et al., 1992). In Scotland, for every herd with a confirmed bTB breakdown, there were more than 20 herds that disclosed at least one unconfirmed reactor through routine herd surveillance. Given the low sensitivity of ante-mortem and post-mortem diagnostics (Norby et al., 2004; de la Rua-Domenech et al., 2006), it can be difficult for regulatory officials to decide whether these herds were truly infected with bTB and should be subject to the same local disease eradication measures as confirmed breakdowns. There are significant costs associated with follow-up testing, contact tracing, and movement restrictions in these unconfirmed herds. Consequently, there have been recent efforts to optimize resource allocation through risk-based surveillance strategies (Bessell et al., 2013). From a broader perspective, these findings highlight that the optimal strategies for endemic disease control are likely to change over the course of an eradication programme and must be factored into simulation models used to support policy decisions.

Reducing network contacts

While there have been many published studies describing the epidemiological consequences of cattle movement network structure, the analyses presented in Chapter 6 are the first to my knowledge that attempt to describe its causes. One of the most important contributions this thesis has made is establishing

a direct relationship between poor herd performance and the risk of purchasing replacement breeding cattle. Herds with high calf mortality rates, abnormal culling rates, prolonged calving intervals, and high average ages at first calving are not only losing significant profit, but also contributing to the persistence of endemic disease in the cattle industry by purchasing excess numbers of replacement breeding cattle. From a theoretical perspective, these movements have a disproportionately strong influence on network transmission dynamics due to their higher betweenness centrality. Any management interventions that can reduce their numbers are therefore likely to be highly effective in preventing the spread of multiple endemic pathogens simultaneously. It has also been suggested that herds with poor performance must maintain larger pools of replacement heifers (Santarossa et al., 2004), which may contribute to the persistence of disease in the herd following an outbreak due to the higher stocking densities. There is need for further research to investigate the impact of poor performance on herd demographic structure and within-herd disease transmission dynamics.

Descriptive statistics on the reproductive performance of breeding cattle highlight the extent to which poor herd management is also undermining the sustainability of British beef and dairy production. Compared with other competitor nations, many herds are failing to meet key industry targets for average age at first calving, calving intervals, culling rates, and calf mortality rates. Previous work by Stott and colleagues (1999) estimated that infertility costs dairy farmers an average of £120 per cow per year, which greatly exceeds the costs of all infectious endemic diseases studied by Bennett and colleagues (1999b). The challenge in this approach lies in being able to identify the cause of poor performance and working with farmers to set realistic targets for improvement. In some cases, the drop in performance may itself be caused by the presence of infectious disease introduced through purchased cattle or other forms of transmission, as highlighted by the result from Chapter 5. Although there are limitations in using the CTS database to calculate reproductive performance benchmarks, it offers the advantage of being able to compare all herds and all animals in the British cattle industry on equal

grounds. This may be useful in identifying particular herd types or regions to target with management surveys and other livestock extension services.

Altering network topology

The concept of restricting cattle trade to prevent disease transmission is by no means new in veterinary epidemiology (Fèvre et al., 2006). However, movement restrictions have historically been reactionary to disease outbreaks and aimed at preventing infected herds from spreading disease through subsequent cattle movements. The approach of intentionally altering network topology by placing restrictions on who individual farmers can trade with represents a novel strategy for pre-emptively controlling disease spread at the industry level. Of all the approaches tested, the most effective was to prevent contacts with a high predicted betweenness centrality. In the real world, this primarily translates into preventing farms with a high in-degree (those most likely to have acquired disease) from selling cattle to farms with a high out-degree (those most likely to subsequently spread disease), although other factors such as herd type, movement distance, and whether the edge was reciprocal or repeated also had an influence on risk. The latter finding suggests that promoting stability in trade relationships over time may be another effective strategy for limiting disease spread. Given the significant promise in these network-based approaches, it is worth investing time in developing more sophisticated models to evaluate the relative costs and benefits of restricting cattle trade.

The basic approach for generating contact networks developed in Chapter 7 can easily be modified to address other important epidemiological questions. For instance, there has been growing interest in using trade regionalization as a means of containing geographically limited diseases (Livingstone et al., 2006). The network generation model provides a framework for exploring how the resulting changes in patterns may influence the transmission dynamics of the disease of interest as well as others spreading through the same contact network. It is worth noting, however, that restricting trade within livestock production zones or network communities appears to have little impact on disease prevalence. This is most likely because the network communities are sufficiently large to sustain disease transmission. Another

important open question is how to build representative contact networks in countries where livestock movements are not centrally recorded. Recent efforts have been made to characterize livestock contact structures in Somalia (Ortiz-Pelaez et al., 2010), Ethiopia (Waret-Szukuta et al., 2010), and Cambodia (Van Kerkhove et al., 2009) through cross-sectional surveys of rural villagers, dealers, and markets. These data could be used to assign farms a degree distribution and to generate rules for contact formation that would feed directly into network generation algorithm. It may be possible to use movement data from the United Kingdom to study the potential biases in generating networks from "sampled" farms with the caveat that trends here may not reflect those in other cattle industries. Some work regarding the issue of missing links and extrapolating networks from sampled links has already been conducted on cattle movement networks in the United States (Lindström et al., 2013) as well as for other types of social netwrks (Clauset et al., 2008; Guimera and Sales-Pardo, 2009).

Farmer behavioural feedback

One of the dangers in implementing mandatory national disease control programmes is that farmers will often change their behaviour in unpredictable ways to mitigate the financial consequences on their business. In the case of Scotland's post-movement testing requirements for bTB, the effect has been a dramatic reduction in the number of cattle imported from high incidence regions, which has likely done as much, if not more, to reduce the risk of disease introductions as the testing itself. Vernon and Keeling (2012) caution, however, that the protective effects are often transient due to ergodic nature of cattle trade networks. This tendency for livestock movement networks to return to their original state was first described by Kao and colleagues (2006). There have been other examples where disease control measures have had unintended negative consequences because of subsequent changes in industry trade patterns. For instance, when Saudi Arabia issued an import ban on livestock products from eastern Africa to control rift valley fever, many livestock were diverted through neighboring countries, which resulted in disease spreading to previously uninfected populations (Soumaré et al., 2006). In

the United Kingdom, farms that restocked following the mandatory culls during the FMD outbreak were significantly more likely experience subsequent bTB breakdowns (Carrique-Mas et al., 2008) and this may have been responsible for disease incursions into low incidence regions.

Other external market forces are also likely to play an important role in shaping future network transmission dynamics through their effects on farmer behaviour. One well-documented example is the cattle cycle during which the numbers of cattle are alternatively expanded and reduced over consecutive years as farmers respond to changes in market prices (Hamilton and Kastens, 2000; Aadland, 2004). When the market value of store cattle is high, farmers are under incentive to maximize profit by increasing breeding herd size and subsequent offtake rates. With the long gestation and maturation period of cattle, there is a two to four year delay before population numbers significantly increase during which time market prices are gradually driven down by the increase in supply. Farmers then collectively respond by decreasing breeding herd size, which causes the cycle to repeat again.

Based on monthly time series data from CTS, it appears that the British cattle industry is in the latter phase, although some of the observed effect may be due to recent changes in agricultural subsidization schemes. Faced with rising costs and declining profits, the cattle industry is moving towards fewer, but larger, farms to capture economies of scale. Brooks-Pollock and Keeling (2009) noted a 16.3% decline in active cattle farms and 17.9% increase in average farm size in Great Britain between 2002 and 2007. Both trends are an epidemiological concern given that short-term expansion is most often achieved by purchasing in additional cattle rather than relying on internal herd growth. There have been several published economic models to predict how farmers should optimize their business in response to market prices or agricultural subsidy reforms (Dunne et al., 2001; Veysset et al., 2005; Matthews et al., 2006), which may be useful to integrate with future dynamic network generation models.

A final source of dynamic behavioural change to consider is farmer response to growing consumer concerns over food safety and animal welfare. One of the

primary reasons Canadian dairy farmers enrolled in a voluntary Johne's disease control program was fear that any link between the causative agent *Mycobacterium avium* ssp. *paratuberculosis and Crohn's disease in humans* would cause consumers to purchase less milk (Sorge et al., 2010). These kinds of socioeconomic drives may be beneficial in improving farmer compliance with biosecurity recommendations in the future.

Alternate transmission routes

Somewhat ironically, one of the most valuable insights to emerge from studying endemic disease transmission through cattle movement networks is that movements rarely explain all of the observed variation in epidemiological patterns (Liu et al., 2007; Green et al., 2008; Dommergues et al., 2012). For many endemic diseases, there is a particular risk associated with having other infected farms in close proximity; however, the precise mechanisms of disease transmission remain elusive. A major impediment to epidemiological risk factor studies is the lack of comprehensive disease surveillance data to establish which farms were potentially infectious contacts. Some work was recently conducted by Garcia Alvarez and colleagues (2011) to link dairy farms with *Staphylococcus aureus* mastitis through both molecular sequencing and contact network analysis. Although these farms were spatially clustered, it was still difficult to identify important local transmission pathways since many of the farms also had frequent contact with other farms outside the cluster. Furthermore, since endemic diseases operate over much longer time scales, the original infectious animal or contact may no longer be present by the time the outbreak is recognized (Fischer et al., 2005; Clegg et al., 2008) . In the future, the ability to reconstruct transmission chains through low cost sequencing technologies may provide additional insight on the types of contacts that facilitate disease transmission (Plucinski et al., 2011; Shirley et al., 2011; Stack et al., 2013).

Another significant challenge is that the risk factors for local transmission are inherently more difficult to describe and quantify than risk factors such as cattle movements. As highlighted by Nespeca and colleagues (1997), the information provided by farmers on biosecurity surveys does not always reflect the true practices

being implemented on the farm. Brennan and colleagues (2008) also found, for example, that over half of boundary fences that farmers perceived to be effective in preventing contact with neighbouring herds still allowed nose-to-nose interactions between cattle. Simple binary 'yes' or 'no' questions, such as those used in the BVDV management surveys, also fail to capture other important information on the frequency, strength, and duration of local contacts. This has several important implications both from a modelling perspective and a control perspective. Although a few studies have included local contacts as edges in the network (Webb, 2005; Dommergues et al., 2012; Garcia Alvarez et al., 2011), there are no validated means of weighting the edges according to their importance other than relying on expert guesses. Furthermore, without good quantitative support for the role of different transmission mechanisms in disease spread, it may be difficult to convince farmers of the need for improved biosecurity, especially since many of the recommended interventions are perceived to be costly and impractical (Bennett and Cooke, 2005). One final complication highlighted by the results from Chapter 4 was that the potential for disease transmission through local mechanisms are likely to be greater for dairy herds than for beef herds simply because dairy cattle are managed more intensively. Any future national disease control programme should account for heterogeneities in herd production type.

Study limitations

The analyses in this thesis were based entirely on secondary data collected through national animal health programmes and smaller surveillance studies. While this approach enables researchers to answer high-impact questions without having to invest significant time and resources in primary data collection (Smith et al., 2011), there are limitations in using the data for purposes beyond its original scope. Here there were particular challenges associated with the lack of comprehensive production information in the CTS database and the inconsistencies in how farm businesses were identified between the different databases. More generally, the scarcity of data on disease transmission parameters and factors motivating farmer

trade behaviour made it difficult to develop more sophisticated network simulation models. This highlights important opportunities for improving the quality and scope of data collected in future epidemiological investigations.

Data limitations

The ability to accurately describe the demographic structure of the cattle industry is fundamental to modelling the spread and control of infectious disease. Although the CTS database provides an unprecedented amount of demographic information on individual cattle and herds, it was originally designed for use in slaughter contact tracing investigations. This thesis highlights three significant limitations in its use for other epidemiological purposes.

First, farmers are not required to report abortions, births of stillborn calves, births of calves that die shortly after birth, movements to and from common grazing pastures, and movements between linked premises. The first three events are potentially important indicators of infectious disease outbreaks or other serious management deficiencies, while the latter two events are potentially import local contact mechanisms (Vernon et al., 2010). This, combined with the time delays in reporting movements, also limits the use of CTS records to monitor spatial and temporal trends in performance that may serve as early indicators of exotic animal disease incursions (Carpenter, 2001; Perrin et al., 2012).

Second, farmers are not required to declare the production type of their farm (i.e., beef suckler, dairy, heifer rearer, dealer, or fattening), the intended production purpose of individual animals (i.e., breeding female, bull, or fattening animal) or the reason for the each cattle movement (i.e. purchased breeding replacement, involuntary cull, or movement to seasonal grazing pasture). This led to particular challenges in distinguishing bulls and culled replacement breeding heifers from cattle that were bred intentionally for fattening. It would be relatively easy to introduce these three additional fields into the CTS database and would provide highly valuable information to support further research into the drivers of contact network structure.

Third, difficulties were also encountered in linking farm data from the VETNET databases, June Agricultural Census, and the BVDV survey studies with farm data from the CTS database. This is primarily because a single farm business may house cattle on multiple uniquely identified locations, but the surveillance and survey results are reported under the main farm CPH code. Although BCMS maintains a record of premises linked to a single farm business, this information is not routinely available to researchers. In general, developing more uniform standards for recording farm-level data will become increasingly more important as the number and complexity of epidemiological data sources grows (Paiba et al., 2007).

Model limitations

Epidemiological models have frequently been criticized for making simplifying assumptions about the many complex processes driving disease transmission dynamics. Current network-based approaches have addressed the problems of assuming that all farms in the population have uniform contact rates and mix homogeneously by using real data on cattle movements to inform simulation models. However, as the preliminary analyses from Chapter 8 demonstrate, these models are still limited in assuming that all edges carry the same risk of spreading disease and that all farms have the same within-herd transmission dynamics. This is inherently related to the scarcity of animal-level disease data to provide robust weights to individual animal movements as well as the scarcity of herd-level disease and demographic data to parameterize simulation models. The former could be solved by sampling individual cattle at markets to determine the prevalence of and risk factors for endemic disease in traded cattle. The latter represents a greater challenge because of the potentially significant delay between disease introduction and detection as well as the significant expense of serially testing cattle in the herd. Furthermore, a large number of herds would likely need to be recruited to capture the effects of heterogeneity in herd structure and management on transmission dynamics.

Previous studies have already established that static network representations fail to capture many important dynamic features of cattle movement networks such as the precise timing of movements on and off farms (Dubé et al., 2008; Vernon and Keeling, 2009). Yet these measures are still widely reported in the literature and used to make inferences about disease transmission dynamics and changes in disease risk over time (Mweu et al., 2013). The network generation model presented in Chapter 7 allowed exploration of these complex relationships in further detail. Although there was a positive correlation between the size of the GSCC and endemic prevalence, there were cases where two networks had virtually identical GSCCs, but vastly different endemic prevalences and cases where two networks had vastly different GSCCs, but virtually identical estimates for endemic prevalence. In every case, it was impossible vary any single network property in isolation, which makes it difficult to tell what was driving the observed differences in transmission dynamics. This led to the conclusion that while static network measures provide a means of describing network structure, dynamic simulation models should be the gold standard to account for all of their interactive effects on disease transmission dynamics.

Future directions

With the increasing availability of high-performance computing and high-resolution epidemiological data, there is almost no limit to the complexities that can be introduced into simulation models. The real challenge for veterinary researchers lies in translating the resulting scientific discoveries into practical interventions that will ultimately reduce the burden of endemic disease on cattle production systems. Results from the BVDV survey studies provide additional evidence of the significant gap between best practice recommendations for disease control and measures that farmers are actually implementing in the field. This is partly attributable to the fact that research outputs are rarely presented in an accessible format. Most farmers, veterinarians, and policy makers do not have ready access to the scientific literature and when they do, the findings are either written in highly technical language or

difficult to apply to an individual herd's unique situation. For example, Stott (2003) quotes a farmer saying that "If the published costs of all the animal diseases on my farm were correct, then I would have gone out of business long ago." Epidemiological models have been criticized in the past for using oversimplified or inappropriate means of estimating the financial burden of disease (McInerney, 1996).

Computerized decision support systems are an important tool that allows farmers to take direct ownership of scientific knowledge without having to invest substantial time in reviewing technical literature (van Schaik et al., 2001; Bennett et al., 2012). Traditionally, these systems provide an interface where users can enter specific information about the farm characteristics and production costs. Then, based on an underlying data-driven model, the user can explore various 'what if' scenarios for preventing and controlling disease in their herd. Bennett and colleagues (2012) emphasize that the model outputs should be realistic and capable of generating discussion with the veterinary surgeon. There are also broader uses of decision support systems in agricultural economics to help farmers determine the financially optimal structure for their herd (Gartner, 1981; Vargas et al., 2001; Demeter et al., 2011) and to optimize replacement breeding cattle policies (Korver and Renkema, 1979; Sol et al., 1984; Heikkilä et al., 2008), which is immediately relevant to the research presented in Chapter 6 on reducing network contacts through improved herd management.

Despite their tremendous value, decision support systems have historically been difficult to disseminate in the cattle industry. It is easy to envision how the CTS database could be used to improve access to the models as well as to improve the quality of their outputs. Most farmers in the United Kingdom have an online account to report cattle movements to BCMS and to obtain up-to-date records of individual animals present on the farm. These data could be directly downloaded into the simulation models through tools provided on the CTS website and used to generate tailored recommendations for disease control, such as the optimal number or even the individual identity of animals to screen as part of risk-based surveillance

programmes. As a specific example, the system could be used to generate automatic reminders to test newborn calves for persistent BVDV infections if the dams were purchased as pregnant breeding replacements. With the models managed in a central location, they could also be easily updated over time to reflect changes in the diagnostic tests, vaccines, and treatments used to support disease control efforts. Thus, farmers would have access to the latest developments in epidemiological research to make more informed management decisions.

Conclusion

Endemic diseases continue to undermine the sustainability of modern cattle production systems despite tremendous advances in our understanding of their important epidemiological features. Major barriers to control include the large number of potentially infectious contacts between herds, the lack of affordable and accurate diagnostic methods to identify infected individuals, and the difficulty in motivating farmers with diverse priorities to take collective action against the spread of disease. With the increasing availability of high-resolution demographic data and high-performance computing, there are many opportunities to develop more targeted and cost-effective approaches to controlling disease at the herd and industry levels. These efforts will require further research into the socioeconomic factors driving farmer behaviour to better inform traditional epidemiological models and close collaboration with industry stakeholders to ensure the research outputs are delivered in an accessible and user-friendly fashion.

.

Bibliography

Aadland, D., 2004. Cattle cycles, heterogeneous expectations, and the age distribution of capital. Journal of Economic Dynamics and Control 28, 1977 - 2002.

Abernethy, D.A., Moscard-Costello, J., Dickson, E., Harwood, R., Burns, K., McKillop, E., McDowell, S., Pfeiffer, D.U., 2011. Epidemiology and management of a bovine brucellosis cluster in Northern Ireland. Preventive Veterinary Medicine 98, 223-229.

Abernethy, D.A., Upton, P., Higgins, I.M., McGrath, G., Goodchild, A.V., Rolfe, S.J., Broughan, J.M., Downs, S.H., Clifton-Hadley, R., Menzies, F.D., de la Rua-Domenech, R., Blissitt, M.J., Duignan, A., More, S.J., 2013. Bovine tuberculosis trends in the UK and the Republic of Ireland, 1995-2010. The Veterinary Record 172, 312.

Ackermann, M., Engels, M., 2006. Pro and contra IBR-eradication. Veterinary Microbiology 113, 293-302.

Ackermann, M., Müller, H.K., Bruckner, L., Kihm, U., 1990. Eradication of infectious bovine rhinotracheitis in Switzerland: review and prospects. Veterinary Microbiology 23, 365-370.

Alban, L., Stryhn, H., Kjedlsen, A.M., Ersboll, A.K., Skjoth, F., Christensen, J., Bitsch, V., Chriel, M., Stroger, U., 2001. Estimating transfer of bovine virus-diarrhoea virus in Danish cattle herds by use of register data. Preventive Veterinary Medicine 52, 133 - 146.

Albert, R., Jeong, H., Barabasi, A.-L., 2000. Error and attack tolerance of complex networks. Nature 406, 378-382.

Amer, P.W., Simm, G., Keane, M.G., Diskin, M.G., Wickham, B.W., 2001. Breeding objectives for beef cattle in Ireland. Livestock Production Science 67, 223 - 239.

Ames, G.M., George, D.B., Hampson, C.P., Kanarek, A.R., McBee, C.D., Lockwood, D.R., Achter, J.D., Webb, C.T., 2011. Using network properties to predict disease dynamics on human contact networks. Proceedings of the Royal Society B 278, 3544 - 3550.

Anderson, R.M., May, R.M., 1991. Infectious diseases of humans: dynamics and control. Oxford Scientific Press.

Anonymous, 2006. Regulatory Impact Assessment: Pre-Movement Testing in England.

Anonymous, 2013. The Scottish BVD Eradication Scheme. Available at: http://www.scotland.gov.uk/Topics/farmingrural/Agriculture/animal-welfare/Diseases/disease/bvd/eradication

Aranez, A., De juan, L., Bezos, J., Alvarez, J., Romero, B., Lozano, F., Paramio, J.L., Lopez-Sanchez, J., Mateos, A., Dominguez, L., 2006. Assessment of diagnostic tools for eradication of bovine tuberculosis in cattle co-infected with *Mycobacterium bovis* and *M. avium* subsp. *paratuberculosis*. Veterinary Research 37, 593 - 606.

Aznar, M.N., Stevenson, M.A., Zarich, L., León, E.A., 2011. Analysis of cattle movements in Argentina, 2005. Preventive Veterinary Medicine 98, 119-127.

Bachofen, C., Braun, U., Hilbe, M., Ehrensperger, F., Stalder, H., Peterhans, E., 2010. Clinical appearance and pathology of cattle persistently infected with bovine viral diarrhoea virus of different genetic subgroups. Veterinary Microbiology 141, 258-267.

Badham, J., Stocker, R., 2010. The impact of network clustering and assortativity on epidemic behaviour. Theoretical Population Biology 77, 71-75.

Bajardi, P., Barrat, A., Natale, F., Savini, L., Colizza, V., 2011. Dynamical patterns of cattle trade movements. PLoS One 6, e19869.

Baptista, F.M., Nunes, T., 2007. Spatial analysis of cattle movement patterns in Portugal. Veterinaria Italiana 43, 611-619.

Barabasi, A.-L., 2009. Scale-Free Networks: A Decade and Beyond. Science 325, 412-413.

Barabasi, A.-L., Albert, R., 1999. Emergence of Scaling in Random Networks. Science 286, 509-512.

Barabási, A.-L., 2009. Scale-Free Networks: A Decade and Beyond. Science 325, 412-413.

Barabási, A.-L., Albert, R., 1999. Emergence of Scaling in Random Networks. Science 286, 509-512.

Barlow, N.D., Kean, J.M., Hickling, G., Livingstone, P.G., Robson, A.B., 1997. A simulation model for the spread of bovine tuberculosis within New Zealand cattle herds. Preventive Veterinary Medicine 32, 57-75.

Bascom, S.S., Young, A.J., 1998. A Summary of the Reasons Why Farmers Cull Cows. Journal of Dairy Science 81, 2299-2305.

Bastida, F., Juste, R., 2011. Paratuberculosis control: a review with a focus on vaccination. Journal of Immune Based Therapies and Vaccines 9, 8.

Bates, T.W., Thurmond, M.C., Carpenter, T.E., 2001. Direct and indirect contact rates among beef, dairy, goat, sheep, and swine herds in three California counties, with reference to control of potential foot-and-mouth disease transmission. American Journal of Veterinary Research 62, 1121-1129.

Beaudeau, F., Assié, S., Seegers, H., Belloc, C., Selial, E., Joly, A., 2001. Assessing the within-herd prevalence of cows antibody-positive to bovine viral diarrhoea virus with a blocking ELISA on bulk tank milk. Veterinary Record 149, 236-240.

Bennett, R., Christiansen, K., Clifton-Hadley, R., 1999a. Preliminary estimates of the direct costs associated with endemic diseases of livestock in Great Britain. Preventive Veterinary Medicine 39, 155-171.

Bennett, R., Cooke, R., 2005. Control of bovine TB: preferences of farmers who have suffered a TB breakdown. Veterinary Record 156, 143 - 145.

Bennett, R., McClement, I., McFarlane, I., 2012. Modelling of Johne's disease control options in beef cattle: A decision support approach. Livestock Science 146, 149-159.

Bennett, R.M., 2009. Farm costs associated with premovement testing for bovine tuberculosis. Veterinary Record 164, 77 - 79.

Bennett, R.M., Christiansen, K., Clifton-Hadley, R.S., 1999b. Estimating the costs associated with endemic diseases of dairy cattle. Journal of Dairy Research 66, 455 - 459.

Berry, D.P., Cromie, A.R., 2009. Associations between age at first calving and subsequent performance in Irish spring calving Holstein-Fresian dairy cows. Livestock Science 123, 44 - 54.

Bessell, P.R., Orton, R., O'Hare, A., Mellor, D.J., Logue, D., Kao, R.R., 2013. Developing a framework for risk-based surveillance of tuberculosis in cattle: a case study of its application in Scotland. Epidemiology and Infection 141, 314 - 323.

Bicknell, K.B., Wilen, J.E., Howitt, R.E., 1999. Public Policy and Private Incentives for Livestock Disease Control. Australian Journal of Agricultural and Resource Economics 43, 501-521.

Bigras-Poulin, M., Barfod, K., Mortensen, S., Greiner, M., 2007. Relationship of trade patterns of the Danish swine industry animal movements network to potential disease spread. Preventive Veterinary Medicine 80, 143-165.

Bigras-Poulin, M., Thompson, R.A., Chriel, M., Mortensen, S., Greiner, M., 2006. Network analysis of Danish cattle industry trade patterns as an evaluation of risk potential for disease spread. Preventive Veterinary Medicine 76, 11-39.

Billinis, C., Leontides, L., Amiridis, G.S., Spyrou, V., Kostoulas, P., Sofia, M., 2005. Prevalence of BVDV infection in Greek dairy herds. Preventive Veterinary Medicine 72, 75-79.

Bitsch, V., Hansen, K.E.L., Rønsholt, L., 2000. Experiences from the Danish programme for eradication of bovine virus diarrhoea (BVD) 1994–1998 with special reference to legislation and causes of infection. Veterinary Microbiology 77, 137-143.

Boily, M.C., Asghar, Z., Garske, T., Ghani, A.C., Poulin, R., 2007. Influence of Selected Formation Rules for Finite Population Networks with Fixed Macrostructures: Implications for Individual-Based Model of Infectious Diseases. Mathematical Population Studies 14, 237-267.

Bonacich, P., Lloyd, P., 2001. Eigenvector-like measures of centrality for asymmetric relations. Social Networks 23, 191-201.

Booth, R.E., Cranwell, M.P., Brownlie, J., 2013. Monitoring the bulk milk antibody response to BVDV: the effects of vaccination and herd infection status. Veterinary Record 172, 449-449.

Bourdon, R., Brinks, J., 1983. Calving date versus calving interval as a reproductive measure in beef cattle. Journal of Animal Science 57, 1412 - 1417.

Brennan, M.L., Christley, R.M., 2012. Bisoecurity on cattle farms: a study in north-west England. PLoS ONE 7, e28139.

Brennan, M.L., Kemp, R., Christley, R.M., 2008. Direct and indirect contacts between cattle farms in north-west England. Preventive Veterinary Medicine 84, 242-260.

Brickell, J.S., McGowan, M.M., Pfeiffer, D.U., Wathes, D.C., 2009. Mortality in Holstein-Friesian calves and replacement heifers, in relation to body weight and IGF-1 concentration, in 19 farms in England. Animal 3, 1175 - 1182.

Brinkhof, J., Zimmer, G., Westenbrink, F., 1996. Comparative study on four enzyme-linked immunosorbent assays and a cocultivation assay for the detection of antigens associated with the bovine viral diarrhoea virus in persistently infected cattle. Veterinary Microbiology 50, 1-6.

Britt, J.H., 1985. Enhanced Reproduction and Its Economic Implications. Journal of Dairy Science 68, 1585-1592.

Brooks-Pollock, E., Keeling, M., 2009. Herd size and bovine tuberculosis persistence in cattle farms in Great Britain. Preventive Veterinary Medicine 92, 360-365.

Brownlie, T.S., Weir, A.M., Tarbotton, I., Morton, J.M., Heuer, C., McDougall, S., 2011. Reporductive management of dairy herds in New Zealand: attitudes, priorities, and constraints percevied by farmers managing seasonal-calving, pasture-based herds in four regions. New Zealand Veterinary Journal 59.

Brulisauer, F., Lewis, F.I., Ganser, A.G., McKendrick, I.J., Gunn, G.J., 2010. The prevalence of bovine viral diarrhoea virus infection in beef suckler herds in Scotland. Veterinary Journal 186, 226 - 231.

Bruzzi, P., Green, S.B., Byar, D.P., Brinton, L.A., Schairer, C., 1985. Estimating the population attributable risk for multiple risk factors using case-control data. American Journal of Epidemiology 122, 904 - 914.

Byrne, D., 1992. Analysis of post-mortem data on tuberculin reactor cattle. Irish Veterinary Journal 45, 131 - 132.

Caldow, G., Lowman, B., Riddell, I., 2005. Farm Animal Practice: Veterinary intervention in the reproductive management of beef cow herds. In Practice 27, 406 - 411.

Caporale, V., Giovannini, A., Di Francesco, C., Calistri, P., 2001. Importance of the traceability of animals and animal products in epidemiology. Revue scientifique et technique (International Office of Epizootics) 20, 372-378.

Caraviello, D.Z., Weigel, K.A., Fricke, P.M., Wiltbank, M.C., Florent, M.J., Cook, N.B., Nordlund, K.V., Zwald, N.R., Rawson, C.L., 2006. Survey of Management Practices on Reproductive Performance of Dairy Cattle on Large US Commercial Farms. Journal of Dairy Science 89, 4723-4735.

Carpenter, T.E., 2001. Methods to investigate spatial and temporal clustering in veterinary epidemiology. Preventive Veterinary Medicine 48, 303-320.

Carpenter, T.E., Chrièl, M., Greiner, M., 2007. An analysis of an early-warning system to reduce abortions in dairy cattle in Denmark incorporating both financial and epidemiologic aspects. Preventive Veterinary Medicine 78, 1-11.

Carrique-Mas, J.J., Medley, G.F., Green, L.E., 2008. Risks for bovine tuberculosis in British cattle farms restocked after the foot and mouth disease epidemic of 2001. Preventive Veterinary Medicine 84, 85-93.

Carslake, D., Grant, W., Green, L.E., Cave, J., Greaves, J., Keeling, M., McEldowney, J., Weldegebriel, H., Medley, G.F., 2011. Endemic cattle diseases: comparative epidemiology and governance. Philosophical Transactions of the Royal Society B: Biological Sciences 366, 1975-1986.

Cherry, B.R., Reeves, M.J., Smith, G., 1998. Evaluation of bovine viral diarrhea virus control using a mathematical model of infection dynamics. Preventive Veterinary Medicine 33, 91 - 108.

Chi, J., VanLeeuwen, J.A., Weersink, A., Keefe, G.P., 2002. Management factors related to seroprevalences to bovine viral-diarrhoea virus, bovine-leukosis virus, Mycobacterium avium subspecies paratuberculosis, and Neospora caninum in dairy herds in the Canadian Maritimes. Preventive Veterinary Medicine 55, 57-68.

Christley, R.M., Robinson, S.E., Moore, B., Setzkorn, C., Donald, I., 2011. Responses of farmers to introduction in England and Wales of pre-movement testing for bovine tuberculosis. Preventive Veterinary Medicine 100, 126 - 133.

Clauset, A., Moore, C., Newman, M.E.J., 2008. Hierarchical structure and the prediction of missing links in networks. Nature 453, 98-101.

Clegg, T., Duignan, A., Whelan, C., Gormley, E., Good, M., Clarke, J., Toft, N., More, S., 2011. Using latent class analysis to estimate the test characteristics of the interferon-y test, the single intradermal comparative tuberculin test and a multiplex immunoassay under Irish conditions. Veterinary Microbiology 151, 68-76.

Clegg, T.A., More, S.J., Higgins, I.M., Good, M., Blake, M., Williams, D.H., 2008. Potential infection-control benefit for Ireland from pre-movement testing of cattle for tuberculosis. Preventive Veterinary Medicine 84, 94-111.

Corner, L.A., 1994. Post mortem diagnosis of Mycobacterium bovis infection in cattle. Veterinary Microbiology 40, 53-63.

Corner, L.A., Melville, L., McCubbin, K., Small, K.J., McCormick, B.S., Wood, P.R., Rothel, J.S., 1990. Efficiency of inspection procedures for the detection of tuberculous lesions in cattle. Australian Veterinary Journal 67, 389 - 392.

Costello, E., Egan, J.W.A., Quigley, F.C., O'Reilly, P.F., 1997. Performance of the single intradermal comparative tuberculin test in identifying cattle with tuberculous lesions in Irish herds. Veterinary Record 141, 222-224.

Courcoul, A., Ezanno, P., 2010. Modelling the spread of Bovine Viral Diarrhoea Virus (BVDV) in a managed metapopulation of cattle herds. Veterinary Microbiology 142, 119-128.

Cousins, D.V., Roberts, J.L., 2001. Australia's campaign to eradicate bovine tuberculosis: the battle for freedom and beyond. Tuberculosis 81, 5-15.

Cowley, D.J.B., Clegg, T.A., Doherty, M.L., More, S.J., 2012. Bovine viral diarrhoea virus seroprevlaence and vaccination usage in dairy and beef herds in the Republic of Ireland. Irish Veterinary Journal 65, 16.

Csardi, G., Nepusz, T., 2006. The igraph software package for complex network research. InterJournal Complex Systams 1695.

Dal Zotto, R., Penasa, M., De Marchi, M., Cassandro, M., Lopez-Villalobos, N., Bittante, G., 2009. Use of crossbreeding with beef bulls in dairy herds: effect on age, body weight, price, and market value of calves sold at livestock auctions. Journal of Animal Science 87, 3053 - 3059.

Daniels, M.J., Hutchings, M.R., Allcroft, D.J., McKendrick, I.J., Greig, A., 2002. Risk factors for Johne's disease in Scotland - the results of a survey of farmers. Veterinary Record 150, 135-139.

David, G.P., Crawshaw, T.R., Gunning, R.F., Hibberd, R.C., Lloyd, G.M., Marsh, P.R., 1994. Severe disease in adult dairy cattle in three UK dairy herds associated with BVD virus infection. Veterinary Record 134, 468 - 472.

de Faria Naves, J.H.F., Rezende, L.M., Ramos, G.C., Soares, P.M., Tavares, T.C.F., França, A.M.S., Neves, S.M.N., Silva, N.A.M., Lima-Ribeiro, A.M.C., 2012. Interference in diagnostic tests for brucellosis in cattle recently vaccinated against leptospirosis. Journal of Veterinary Diagnostic Investigation 24, 283-287.

de la Rua-Domenech, R., Goodchild, A.T., Vorermeier, H.M., Hewinson, R.G., Christiansen, K.H., Clifton-Hadley, R.S., 2006. Ante mortem diagnosis of tuberculosis in cattle: a review of the tuberculing tests, y-interferon assay and other ancillary diagnostic techniques. Research in Veterinary Science 81, 190 - 210.

de Vries, A., Risco, C.A., 2005. Trends and Seasonality of Reproductive Performance in Florida and Georgia Dairy Herds from 1976 to 2002. Journal of Dairy Science 88, 3155-3165.

DEFRA, 2012. Bovine tuberculosis. Available at: http://www.defra.gov.uk/animal-diseases/a-z/bovine-tb/

Demeter, R.M., Kristensen, A.R., Djikstra, J., Oude Lansink, A.G.J.M., Meuwissen, M.P.M., van Arendonk, J.A.M., 2011. A multi-level hierarchic Markov process with Bayesian updating for herd optimization and simulation in dairy cattle. Journal of Dairy Science 94, 5938 - 5962.

Diéguez, F.J., Yus, E., Vilar, M.J., Sanjuán, M.L., Arnaiz, I., 2009. Effect of the bovine viral diarrhoea virus (BVDV) infection on dairy calf rearing. Research in Veterinary Science 87, 39-40.

Doherr, M.G., Audige, L., 2001. Monitoring and surveillance for rare health-related events: a review from the veterinary perspective. Phil. Trans. R. Soc. Lond. B 356, 1097 - 1106.

Dommergues, L., Rautureau, S., Petit, E., Dufour, D., 2012. Network of contacts between cattle herds in a French area affected by bovine tuberculosis in 2010. Transboundary and Emerging Diseases 59, 292-302.

Dubé, C., Ribble, C., Kelton, D., McNab, B., 2008. Comparing Network Analysis Measures to Determine Potential Epidemic Size of Highly Contagious Exotic Diseases in Fragmented Monthly Networks of Dairy Cattle Movements in Ontario, Canada. Transboundary and Emerging Diseases 55, 382-392.

Dubé, C., Ribble, C., Kelton, D., McNab, B., 2009. A Review of Network Analysis Terminology and its Application to Foot-and-Mouth Disease Modelling and Policy Development. Transboundary and Emerging Diseases 56, 73-85.

Dubé, C., Ribble, C., Kelton, D., McNab, B., 2011. Estimating potential epidemic size following introduction of a long-incubation disease in scale-free connected networks of milking-cow movements in Ontario, Canada. Preventive Veterinary Medicine *99, 102-111*.

Duncan, A.J., Gunn, G.J., Lewis, F.I., Umstatter, C., Humphry, R.W., 2012. The influence of empirical contact networks on modelling diseases in cattle. Epidemics 4, 117-123.

Dunne, W., O'Neill, R., McEvoy, O., 2001. Economics of cattle production systems post CAP reform. University College Dublin.

Ellis-Iversen, J., Cook, A.J.C., Watson, E., Nielen, M., Larkin, L., Wooldridge, M., Hogeveen, H., 2010. Perceptions, circumstances and motivators that influence implementation of zoonotic control programs on cattle farms. Preventive Veterinary Medicine 93, 276-285.

Ellis-Iversen, J., Smith, R.P., Gibbens, J.C., Sharpe, C.E., Dominguez, M., Cook, A.J.C., 2011. Risk factors for transmission of foot-and-mouth disease during an outbreak in southern England in 2007. Veterinary Record 168, 128.

Ersbøll, A.K., Ersbøll, B.K., Houe, H., Alban, L., Kjeldsen, A.M., 2010. Spatial modelling of the between-herd infection dynamics of bovine virus diarrhoea virus (BVDV) in dairy herds in Denmark. Preventive Veterinary Medicine 97, 83-89.

Ersbøll, A.K., Rugbjerg, H., Stryhn, H., 2003. Increased mortality among calves in Danish cattle herds during bovine virus diarrhoea infection. Acta Veterinaria Scandinavica 44, 49.

Esselmont, R.J., Kossaibati, M.A., 1997. Culling in 50 dairy herds in England. Veterinary Record 140, 36-39.

Ettema, J.F., Santos, J.E.P., 2004. Impact of age at calving on lactation, reproduction, health, and income in first-parity Holsteins on commercial farms. Journal of Dairy Science 87, 2730 - 2742.

Evans, R.D., Wallace, M., Shalloo, L., Garrick, D.J., Dillon, P., 2006. Financial implications of recent declines in reproduction and survival of Holstein-Friesian cows in spring-calving Irish dairy herds. Agricultural Systems 89, 165-183.

Ezanno, P., Fourichon, C., Beaudeau, F., Seegers, H., 2006. Between-herd movements of cattle as a tool for evaluating the risk of introducing infected animals. Animal Research 55, 189-208.

Ezanno, P., Fourichon, C., Seegers, H., 2008. Influence of herd structure and type of virus introduction on the spread of bovine viral diarrhoea virus (BVDV) within a dairy herd. Veterinary Research 39, 39.

Ezanno, P., Fourichon, C., Viet, A.-F., Seegers, H., 2007. Sensitivity analysis to identify key-parameters in modelling the spread of bovine viral diarrhoea virus in a dairy herd. Preventive Veterinary Medicine 80, 49-64.

Faust, M.A., Kinsel, M.L., Kirkpatrick, M.A., 2001. Characterizing biosecurity, health, and culling during dairy herd expansions. Journal of Dairy Science 84, 955 - 965.

Fèvre, E.M., Bronsvoort, B.M.d.C., Hamilton, K.A., Cleaveland, S., 2006. Animal movements and the spread of infectious diseases. Trends in Microbiology 14, 125-131.

Firestone, S.M., Ward, M.P., Christley, R.M., Dhand, N.K., 2011. The importance of location in contact networks: describing early epidemic spread using spatial social network analysis. Preventive Veterinary Medicine 102, 185 - 195.

Fischer, E.A.J., van Roermund, H.J.W., Hemerik, L., van Asseldonk, M.A.P.M., de Jong, M.C.M., 2005. Evaluation of surveillance strategies for bovine tuberculosis (Mycobacterium bovis) using an individual based epidemiological model. Preventive Veterinary Medicine 67, 283-301.

Flaten, O., Lien, G., Koesling, M., Valle, P.S., Ebbesvik, M., 2005. Comparing risk perceptions and risk management in organic and conventional dairy farming: empirical results from Norway. Livestock Production Science 95, 11 - 25.

Fortunato, S., 2010. Community detection in graphs. Physics Reports 486, 75-174.

Fox, L., Kirk, J., Britten, A., 2005. Mycoplasma mastitis: a review of transmission and control. Journal of Veterinary Medicine, Series B 52, 153-160.

Fray, M.D., Paton, D.J., Alenius, S., 2000. The effects of bovine viral diarrhoea virus on cattle reproduction in relation to disease control. Animal Reproduction Science 60–61, 615-627.

Fredriksen, B., Odegaard, S.A., Loken, T., 1998. The effect of bovine virus diarrhoea virus on reproduction in recently infected Norwegian dairy herds. Acta Veterinaria Scandinavica 39, 99 - 108.

Frössling, J., Ohlson, A., Björkman, C., Håkansson, N., Nöremark, M., 2012. Application of network analysis parameters in risk-based surveillance – Examples based on cattle trade data and bovine infections in Sweden. Preventive Veterinary Medicine 105, 202-208.

Fulton, R.W., Whitley, E.M., Johnson, B.J., Ridpath, J.F., Kapil, S., Burge, L.J., Cook, B.J., Confer, A.W., 2009. Prevalence of bovine viral diarrhea virus (BVDV) in persistently infected cattle and BVDV subtypes in affected cattle in beef herds in south central United States. Canadian Journal of Veterinary Research 73, 283 - 291.

Funk, S., Salathe, M., Jansen, V.A.A., 2010. Modelling the influence of human behaviour on the spread of infectious diseases: a review. Journal of the Royal Society Interface 7, 1247 - 1256.

Funston, R.N., Deutscher, G.H., 2004. Comparison of target breeding weight and breeding date for replacement beef heifers and effects on subsequent reproduction and calf performance. Journal of Animal Science 82, 3094-3099.

Garcia Alvarez, R., Webb, C., Holmes, M., 2011. A novel field-based approach to validate the use of network models for disease spread between dairy herds. Epidemiology and Infection 139, 1863 - 1874.

Gartner, J.A., 1981. Replacement policy in dairy herds on farms where heifers compete with the cows for Grassland--part 1: Model construction and validation. Agricultural Systems 7, 289-318.

Gates, M.C., Volkova, V.V., Woolhouse, M.E.J., 2013. Impact of changes in cattle movement regulations on the risks of bovine tuberculosis for Scottish farms. Preventive Veterinary Medicine 108, 125-136.

Gilbert, M., Mitchell, A., Bourn, D., Mawdsley, J., Clifton-Hadley, R., Wint, W., 2005. Cattle movements and bovine tuberculosis in Great Britain. Nature Letters 435, 491 - 496.

Girvan, M., Newman, M.E., 2001. Community structure in social and biological networks. Available at: http://arXiv preprint cond-mat/0112110.

Goodchild, A.V., Clifton-Hadley, R.S., 2001. Cattle-to-cattle transmission of Mycobacterium bovis. Tuberculosis 81, 23 - 41.

Gopal, R., Goodchild, A., Hewinson, G., de la Rua Domenech, R., Clifton-Hadley, R., 2006. Introduction of bovine tuberculosis to north-east England by bought-in cattle. Veterinary Record 159, 265-271.

Gordejo, F.J.R., Verneersch, J.P., 2006. Towards eradication of bovine tuberculosis in the European Union. Veterinary Microbiology 112, 101-109.

Gramig, B.M., Horag, R.D., 2011. Jointly determined livestock disease dynamics and decentralized economic behaviour. Australian Journal of Agricultural and Resource Economics 55, 393 - 410.

Gramig, B.M., Horan, R.D., Wolf, C.A., 2009. Livestock disease indemnity design when moral hazard is followed by adverse selection. American Journal of Agricultural Economics 91, 627 - 641.

Grant, I., 2005. Zoonotic potential of Mycobacterium avium ssp. paratuberculosis: the current position. Journal of Applied Microbiology 98, 1282-1293.

Green, D.M., Gregory, A., Munro, L.A., 2009. Small- and large-scale network structure of live fish movements in Scotland. Preventive Veterinary Medicine 91, 261-269.

Green, D.M., Kao, R.R., 2007. Data quality of the Cattle Tracing System in Great Britain. Veterinary Record 161, 439-443.

Green, D.M., Kiss, I.Z., Kao, R.R., 2006. Modelling the initial spread of foot-and-mouth disease through animal movements. Proceedings. Biological sciences / The Royal Society 273, 2729-2735.

Green, D.M., Kiss, I.Z., Mitchell, A.P., Kao, R.R., 2008. Estimates for local and movement-based transmission of bovine tuberculosis in British cattle. Proceedings. Biological sciences / The Royal Society 275, 1001-1005.

Green, L.E., Carrique-Mas, J.J., Mason, S.A., Medley, G.F., 2012. Patterns of delayed detection and persistence of bovine tuberculosis in confirmed and unconfirmed herd breakdowns in cattle and cattle herds in Great Britain. Preventive Veterinary Medicine 106, 266-274.

Green, L.E., Cornell, S.J., 2005. Investigations of cattle herd breakdowns with bovine tuberculosis in four counties of England and Wales using VETNET data. Preventive Veterinary Medicine 70, 293-311.

Green, L.E., Medley, G.F., 2002. Mathematical modelling of the foot and mouth disease epidemic of 2001: strengths and weaknesses. Research in Veterinary Science 73, 201-205.

Greiser-Wilke, I., Grummer, B., Moennig, V., 2003. Bovine viral diarrhoea eradication and control programmes in Europe. Biologicals 31, 113-118.

Graham, D.A., German, A., McLaren, I.E., Fitzpatrick, D.A., 2001. Testing of bulk tank milk from Northern Ireland dairy herds for viral RNA and antibody to bovine viral diarrhoea virus. Veterinary Record 149, 261-265.

Griffin, J.M., Martin, S.W., Thorburn, M.A., Eves, J.A., Hammond, R.F., 1996. A case-control study on the association of selected risk factors with the occurrence of bovine tuberculosis in the Republic of Ireland. Preventive Veterinary Medicine 27, 217 - 229.

Griffin, J.M., Williams, D.H., Kelly, G.E., Clegg, T.A., O'Boyle, I., Collins, J.D., More, S.J., 2005. The impact of badger removal on the control of tuberculosis in cattle herds in Ireland. Preventive Veterinary Medicine 67, 237-266.

Grisi-Filho, J.H.H., Amaku, M., Ferreira, F., Dias, R.A., Neto, J.S.F., Negreiros, R.L., Ossada, R., 2013. Detecting livestock production zones. Preventive Veterinary Medicine 110, 304-311.

Groenendaal, H., Galligan, D.T., Mulder, H.A., 2004. An Economic Spreadsheet Model to Determine Optimal Breeding and Replacement Decisions for Dairy Cattle. Journal of Dairy Science 87, 2146-2157.

Grohn, Y.T., Rajala-Schultz, P.J., 2000. Epidemiology of reproductive performance in dairy cows. Animal Reproduction Science 60-61, 605 - 614.

Guimera , R., Sales-Pardo, M., 2009. Missing and spurious interactions and the reconstruction of complex networks. Proceedings of the National Academy of Sciences 106, 22073-22078.

Gunn, G.J., Humphry, R.W., Jones, G.J., Stott, A.W., 2003. Estimating the economic losses associated with BVD infection in the UK dairy herd. Acta Veterinaria Scandinavica 44, 228.

Gunn, G.J., Stott, A.W., Humphry, R.W., 2004. Modelling and costing BVD outbreaks in beef herds. The Veterinary Journal 167, 143-149.

Gupta, S., Anderson, R.M., May, R.M., 1989. Networks of sexual contacts: implications for the pattern of spread of HIV. AIDS (London, England) 3, 807-817.

Hadley, G.L., Wolf, C.A., Harsh, S.B., 2006. Dairy cattle culling patterns, explanations, and implications. Journal of Dairy Science 89, 2286 - 2296.

Hakansson, N., Jonsson, A., Lennartsson, J., Lindström, T., Wennergren, U., 2010. Generating structure specific networks. Advances in Complex Systems 13, 239 - 250.

Halliday, J., Chase-Topping, M., Pearce, M., McKendrick, I., Allison, L., Fenlon, D., Low, C., Mellor, D., Gunn, G., Woolhouse, M., 2006. Herd-level risk factors associated with the presence of Phage type 21/28 E. coli O157 on Scottish cattle farms. BMC Microbiology 6, 99.

Hamilton, S.F., Kastens, T.L., 2000. Does market timing contribute to the cattle cycle? American Journal of Agricultural Economics 82, 82 - 96.

Harkness, J.W., Sands, J.J., Richards, M.S., 1978. Serological studies of mucosal disease virus in England and Wales. Research in Veterinary Science 24, 98 - 103.

Haworth, G.M., Tranter, W.P., Chuck, J.N., Cheng, Z., Wathes, D.C., 2008. Relationships between age at first calving and first lactation milk yield, and lifetime productivity and longevity in dairy cows. Veterinary Record 162, 643 - 647.

Heffernan, C., Nielsen, L., Thomson, K., Gunn, G., 2008. An exploration of the drivers to bio-security collective action among a sample of UK cattle and sheep farmers. Preventive Veterinary Medicine 87, 358-372.

Heikkilä, A.M., Nousiainen, J.I., Jauhiainen, L., 2008. Optimal Replacement Policy and Economic Value of Dairy Cows with Diverse Health Status and Production Capacity. Journal of Dairy Science 91, 2342-2352.

Hickson, R.E., Lopez-Villalobos, N., Kenyon, P.R., Ridler, B.J., Morris, S.T., 2010. Profitability of calving heifers at 2 compared with 3 years of age and the effect of incidence of assistance at parturition on profitability. Animal Production Science 50, 354 - 358.

Hobbs, J.E., 1997. Measuring the Importance of Transaction Costs in Cattle Marketing. American Journal of Agricultural Economics 79, 1083-1095.

Hoe, F.G.H., Ruegg, P.L., 2006. Opinions and Practices of Wisconsin Dairy Producers About Biosecurity and Animal Well-Being. Journal of Dairy Science 89, 2297-2308.

Holme, P., Kim, B.J., 2002. Growing scale-free networks with tunable clustering. Physical Review E 65, e026107.

Houe, H., 1992. Age distribution of animals persistently infected with bovine diarrhea virus in twenty-two Danish dairy herds. Canadian Journal of Veterinary Research 56, 194 - 198.

Houe, H., 1993. Survivorship of animals persistently infected with bovine virus diarrhoea virus (BVDV). Preventive Veterinary Medicine 15, 275-283.

Houe, H., 1994. Bovine virus diarrhoea virus: detection of Danish dairy herds with persistently infected animals by means of a screening test of ten young stock. Preventive Veterinary Medicine 19, 241 -248.

Houe, H., 1995. Epidemiology of bovine viral diarrhea virus. Veterinary Clinics of North America: Food Animal Practice 11, 521 - 547.

Houe, H., Baker, J.C., Maes, R.K., Lloyd, J.W., Enevoldsen, C., 1995a. Comparison of the prevalence and incidence of infection with bovine viral diarrhoea virus (BVDV) in Denmark and Michigan and association with possible risk factors. Acta Veterinaria Scandinavica 36, 521 - 531.

Houe, H., Baker, J.C., Maes, R.K., Wuryastuti, H., Wasito, R., Ruegg, P.L., Lloyd, J.W., 1995b. Prevalence of cattle persistently infected with bovine viral diarrhea virus in 20 dairy herds in two counties of central Michigan and comparison of prevalence of antibody positive cattle among herds with different infection and vaccination status. Journal of Veterinary Diagnostic Investigation 7, 321 - 326.

Houe, H., Lindberg, A., Moennig, V., 2006. Test strategies in bovine viral diarrhea virus control and eradication campaigns in Europe. Journal of Veterinary Diagnostic Investigation 18, 427 - 436.

Houe, H., Meyling, A., 1991. Prevalence of bovine virus diarrhoea (BVD) in 19 Danish dairy herds and estimation of incidence of infection in early pregnancy. Preventive Veterinary Medicine 11, 9 - 16.

Huettel, S., Jongeneel, R., 2011. How has the EU milk quota affected patterns of herd-size change? Eurpoean Review of Agricultural Economics 38, 497 - 527.

Hult, L., Lindberg, A., 2005. Experiences from BVDV control in Sweden. Preventive Veterinary Medicine 72, 143-148.

Humblet, M.F., Walravens, K., Salandre, O., Boschiroli, M.L., Gilbert, M., Berkvens, D., Fauville-Dufaux, M., Godfroid, J., Dufey, J., Raskin, A., Vanholme, L., Saegerman, C., 2011. Monitoring of the intra-dermal tuberculosis skin test performed by Belgian field practitioners. Research in Veterinary Science 91, 199-207.

Humphry, R.W., Brulisauer, F., McKendrick, I.J., Nettleton, P.F., Gunn, G.J., 2012. Prevalence of antibodies to bovine viral diarrhoea virus in bulk tank milk and associated risk factors in Scottish dairy herds. Veterinary Record 171, 445.

Innocent, G., Morrison, I., Brownlie, J., Gettinby, G., 1997. A computer simulation of the transmission dynamics and the effects of duration of immunity and survival of persistently infected animals on the spread of bovine viral diarrhoea virus in dairy cattle. Epidemiology and Infection 119, 91 - 100.

Jones, B.A., Grace, D., Kock, R., Alonso, S., Rushton, J., Said, M.Y., McKeever, D., Mutua, F., Young, J., McDermott, J., Pfeiffer, D.U., 2013. Zoonosis emergence linked to agricultural intensification and environmental change. Proceedings of the National Academy of Sciences 110, 8399-8404.

Kahrs, R.F., Scott, F.W., de Lahunta, A., 1970. Congenital cerebellar hypoplasia and ocular defects in calves following bovine viral diarrhea-mucosal disease infection in pregnant cattle. Journal of the American Veterinary Medical Association 156, 1443 - 1450.

Kao, R.R., Danon, L., Green, D.M., Kiss, I.Z., 2006. Demographic structure and pathogen dynamics on the network of livestock movements in Great Britain. Proceedings. Biological sciences / The Royal Society 273, 1999-2007.

Kao, R.R., Green, D.M., Johnson, J., Kiss, I.Z., 2007. Disease dynamics over very different time-scales: foot-and-mouth disease and scrapie on the network of livestock movements in the UK. Journal of the Royal Society Interface 4, 907-916.

Karrer, B., Newman, M.E.J., 2011. Stochastic blockmodels and community structure in networks. Physical Review E 83, e 016107.

Keeling, M.J., 1999. The effects of local spatial structure on epidemiological invasions. Proceedings. Biological sciences / The Royal Society 266, 859-867.

Keeling, M.J., Danon, L., Vernon, M.C., House, T.A., 2010. Individual identity and movement networks for disease metapopulations. Proceedings of the National Academy of Sciences 107, 8866-8870.

Kenah, E., Robins, J.M., 2007a. Network-based analysis of stochastic SIR epidemic models with random and proportionate mixing. Journal of Theoretical Biology 249, 706-722.

Kenah, E., Robins, J.M., 2007b. Second look at the spread of epidemics on networks. Physical Review E 76, e036113.

Kiss, I.Z., Green, D.M., Kao, R.R., 2006. The network of sheep movements within Great Britain: network properties and their implications for infectious disease spread. Journal of the Royal Society Interface 3, 669-677.

Kiss, I.Z., Green, D.M., Kao, R.R., 2008. The effect of network mixing patterns on epidemic dynamics and the efficacy of disease contact tracing. Journal of the Royal Society Interface 5, 791-799.

Korver, S., Renkema, J.A., 1979. Economic evaluation of replacement rates in dairy herds II. Selection of cows during the first lactation. Livestock Production Science 6, 29-37.

Le Cozler, Y., Lollivier, V., Lacasse, P., Disenhaus, C., 2008. Rearing strategy and optimizing first-calving targets in dairy heifers: a review. Animal 2, 1393 - 1404.

Lentz, H.H.K., Konschake, M., Teske, K., Kasper, M., Rother, B., Carmanns, R., Petersen, B., Conraths, F.J., Selhorst, T., 2010. Trade communities and their spatial patterns in the German pork production network. Preventive Veterinary Medicine 98, 176-181.

Leslie, J., Upton, M., 1999. The economic implications of greater global trade in livestock and livestock products. Revue scientifique et technique (International Office of Epizootics) 18, 440 - 457.

Lesmeister, J.L., Burfening, P.J., Blackwell, R.L., 1973. Date of first calving in beef cows and subsequent calf production. Journal of Animal Science 36, 1 - 6.

Levins, R., 1969. Some demographic and genetic consequences of environmental heterogeneity for biological control. Bulletin of the ESA 15, 237-240.

Lindberg, A., Brownlie, J., Gunn, G.J., Houe, H., Moennig, V., Saatkamp, H.W., Sandvik, T., Valle, P.S., 2006. The control of bovine viral diarrhoea virus in Europe: today and in the future. Revue scientifique et technique (International Office of Epizootics) 25, 961 - 979.

Lindberg, A., Houe, H., 2005. Characteristics in the epidemiology of bovine viral diarrhea virus (BVDV) of relevance to control. Preventive Veterinary Medicine 72, 55-73.

Lindberg, A.L.E., Alenius, S., 1999. Principles for eradication of bovine viral diarrhoea virus (BVDV) infections in cattle populations. Veterinary Microbiology 64, 197-222.

Lindström, T., Grear, D.A., Buhnerkempe, M., Webb, C.T., Miller, R.S., Portacci, K., Wennigren, U., 2013. A Bayesian Approach for Modeling Cattle Movements in the United States: Scaling up a Partially Observed Network. PLoS ONE 8, e53432.

Lindström, T., Sisson, S.A., Lewerin, S.S., Wennergren, U., 2010. Bayesian analysis of animal movements related to factors at herd and between herd levels: Implications for disease spread modeling. Preventive Veterinary Medicine 98, 230 - 242.

Lindström, T., Sisson, S.A., Nöremark, M., Jonsson, A., Wennergren, U., 2009. Estimation of distance related probability of animal movements between holdings and implications for disease spread modeling. Preventive Veterinary Medicine 91, 85-94.

Liu, W.C., Matthews, L., Chase-Topping, M., Savill, N.J., Shaw, D.J., Woolhouse, M.E.J., 2007. Metapopulation dynamics of Escherichia coli O157 in cattle: an exploratory model. Journal of the Royal Society Interface 4, 917-924.

Liu, Z., Bambi, H., 2005. Epidemic spreading in community networks. EPL (Europhysics Letters) 72, 315.

Livingstone, P.G., Ryan, T.J., Hancox, N.G., Crews, K.B., Bosson, M.A.J., Knowles, G.J.E., McCook, W., 2006. Regionalisation: A strategy that will assist with bovine tuberculosis control and facilitate trade. Veterinary Microbiology 112, 291-301.

Lombard, J.E., Garry, F.B., Tomlinson, S.M., Garber, L.P., 2007. Impacts of Dystocia on Health and Survival of Dairy Calves. Journal of Dairy Science 90, 1751-1760.

Lucy, M.C., 2001. Reproductive Loss in High-Producing Dairy Cattle: Where Will It End? Journal of Dairy Science 84, 1277-1293.

Luzzago, C., Frigerio, M., Piccinini, R., Dapra, V., Zecconi, A., 2008. A scoring system for risk assessment of the introduction and spread of bovine viral diarrhoea virus in dairy herds in Northern Italy. The Veterinary Journal 177, 236 - 241.

Luzzago, C., Piccinini, R., Zepponi, A., Zecconi, A., 1999. Study on prevalence of bovine viral diarrhoea virus (BVDV) antibodies in 29 Italian dairy herds with reproductive problems. Veterinary Microbiology 64, 247-252.

MacGregor, R.G., Casey, N.H., 1999. Evaluation of calving interval and calving date as measures of reproductive performance in a beef herd. Livestock Production Science 57, 181-191.

Madders, B., 2006. Review of livestock movement controls. London, 36.

Magne, M.A., Cerf, M., Ingrand, S., 2011. Understanding beef-cattle farming management strategies by identifying motivations behind farmers' priorities. Animal 6, 1 - 9.

Mahmood, A.H., Jabbar, A., Egemen, K.C., James, P.G.S., 2010. Deriving network topologies from real world constraints. In, GLOBECOM Workshops (GC Wkshps), 2010 IEEE, 400-404.

Mainar-Jaime, R.C., Berzal-Herranz, B., Arias, P., Rojo-Vázquez, F.A., 2001. Epidemiological pattern and risk factors associated with bovine viral-diarrhoea virus (BVDV) infection in a non-vaccinated dairy-cattle population from the Asturias region of Spain. Preventive Veterinary Medicine 52, 63-73.

Marcé, C., Ezanno, P., Seegers, H., Pfeiffer, D.U., Fourichon, C., 2011. Within-herd contact structure and transmission of Mycobacterium avium subspecies paratuberculosis in a persistently infected dairy cattle herd. Preventive Veterinary Medicine 100, 116-125.

Mars, M.H., Bruschke, C.J.M., van Oirschot, J.T., 1999. Airborne transmission of BHV1, BRSV, and BVDV among cattle is possible under experimental conditions. Veterinary Microbiology 66, 197-207.

Martin, S.W., Shoukri, M., Thorburn, M.A., 1992. Evaluating the health status of herds based on tests applied to individuals. Preventive Veterinary Medicine 14, 33-43.

Martínez-López, B., Perez, A.M., Sánchez-Vizcaíno, J.M., 2009a. Combined application of social network and cluster detection analyses for temporal-spatial characterization of animal movements in Salamanca, Spain. Preventive Veterinary Medicine 91, 29-38.

Martínez-López, B., Perez, A.M., Sánchez-Vizcaíno, J.M., 2009b. Social Network Analysis. Review of General Concepts and Use in Preventive Veterinary Medicine. Transboundary and Emerging Diseases 56, 109-120.

Matthews, K.B., Wright, I.A., Buchan, K., Davies, D.A., Schwarz, G., 2006. Assessing the options for upland livestock systems under CAP reform: developing and applying a livestock systems model within whole-farms system analysis. Agricultural Systems 90, 32 - 61.

May, R.M., Lloyd, A.L., 2001. Infection dynamics on scale-free networks. Physical Review E 64, e066112.

McClurkin, A.W., Coria, M.F., Cutlip, R.C., 1979. Reproductive performance of apparently healthy cattle persistently infected with bovine viral diarrhea virus. Journal of the American Veterinary Medical Association 174, 1116 - 1119.

McClurkin, A.W., Littledike, E.T., Cutlip, R.C., Frank, G.H., Coria, M.F., Bolin, S.R., 1984. Production of cattle immunotolerant to bovine viral diarrhea virus. Canadian Journal of Comparative Medicine 48, 156 - 161.

McDermott, J.J., Allen, O.B., Martin, S.W., 1992. Culling practices of Ontario cow-calf producers. Canadian Journal of Veterinary Research 56, 56 - 61.

McDougall, S., 2006. Reproductive performance and management of dairy cattle. Journal of Reproduction and Development 52, 185 - 194.

McGowan, M.R., Kirkland, P.D., Rodwell, B.J., Kerr, D.R., Carroll, C.L., 1993. A field investigation of the effects of bovine viral diarrhea virus infection around the time of insemination on the reproductive performance of cattle. Theriogenology 39, 443-449.

McInerney, J., 1996. Old economics for new problems - livestock disease: presidential address. Journal of Agricultural Economics 47, 295 - 314.

Mee, J.F., Berry, D.P., Cromie, A.R., 2008. Prevalence of, and risk factors associated with, perinatal calf mortality in pasture-based Holstein-Friesian cows. Animal 2, 613 - 620.

Mee, J.F., Geraghty, T., O'Neill, R., More, S.J., 2012. Bioexclusion of diseases from dairy and beef farms: Risks of introducing infectious agents and risk reduction strategies. The Veterinary Journal 194, 143-150.

Meloni, S., Perra, N., Arenas, A., Gomez, S., Moreno, Y., Vespignani, A., 2011. Modeling human mobility responses to the large-scale spreading of infectious diseases. Scientific Reports. 1, 62.

Menzies, F.D., Neill, S.D., 2000. Cattle-to-Cattle Transmission of Bovine Tuberculosis. The Veterinary Journal 160, 92-106.

Meuwissen, M.P.M., Huirne, R.B.M., Hardaker, J.B., 2001. Risk and risk management: an empirical analysis of Dutch livestock farmers. Livestock Production Science 69, 43 - 53.

Meyling, A., Houe, H., Jensen, A.M., 1990. Epidemiology of bovine virus diarrhoea virus. Revue scientifique et technique (International Office of Epizootics) 9, 75 - 93.

Mitchell, A., Bourn, D., Mawdsley, J., Wint, W., Clifton-Hadley, R., Gilbert, M., 2005. Characteristics of cattle movements in Britain-an analysis of records from the Cattle Tracing System. Animal Science 80, 265 - 273.

Mitchell, A.P.G., L. E.Clifton-Hadley, R.Mawdsley, J.Sayers, R.Medley, G. F., 2006. An analysis of single intradermal comparative cervical test (SICCT) coverage in the GB cattle population. In: Mellor, D.J.R., A. M. (Ed.), Society for Veterinary Epidemiology and Preventive Medicine. Exeter, UK, 70 - 86.

Mockeliūniene ,V., Šalomskas, A., Mockeliūnas, R., Petkevičius, S., 2004. Prevalence and epidemiological features of bovine viral diarrhoea virus infection in Lithuania. Veterinary Microbiology 99, 51-57.

Moerman, A., Straver, P.J., de Jong, M.C.M., Quak, J., Baavinger, T., van Oirschot, T.J., 1994. Clinical consequences of a bovine virus diarrhoea virus infection in a dairy herd: a longitudinal study. Veterinary Quarterly 16, 115 - 119.

Monaghan, M.L., Doherty, M.L., Collins, J.D., Kazda, J.F., Quinn, P.J., 1994. The tuberculin test. Veterinary Microbiology 40, 111-124.

Moore, D., Adaska, J., Higginbotham, G., Castillo, A., Collar, C., Sischo, W., 2009. Testing new dairy cattle for disease can boost herd health, cut costs. California Agriculture 63, 29 - 34.

Moore, D.A., Merryman, M.L., Hartman, M.L., Klingborg, D.J., 2008. Comparison of published recommendations regarding biosecurity practices for various production animal species and classes. Journal of the American Veterinary Medical Association 233, 249 - 256.

Moslonka-Lefebvre, M., Pautasso, M., Jeger, M.J., 2009. Disease spread in small-size directed networks: Epidemic threshold, correlation between links to and from nodes, and clustering. Journal of Theoretical Biology 260, 402-411.

Munroe, F.A., Dohoo, I.R., McNab, W.B., Spangler, L., 1999. Risk factors for the between-herd spread of Mycobacterium bovis in Canadian cattle and cervids between 1985 and 1994. Preventive Veterinary Medicine 41, 119 - 133.

Muñoz Mendoza, M., Juan, L.d., Menéndez, S., Ocampo, A., Mourelo, J., Sáez, J.L., Domínguez, L., Gortázar, C., García Marín, J.F., Balseiro, A., 2012. Tuberculosis due to Mycobacterium bovis and Mycobacterium caprae in sheep. The Veterinary Journal 191, 267-269.

Muñoz-Zanzi, C.A., Hietala, S.K., Thurmond, M.C., Johnson, W.O., 2003. Quantification, risk factors, and health impact of natural congenital infection with bovine viral diarrhea virus in dairy calves. American Journal of Veterinary Research 64, 358-365.

Mweu, M.M., Fournié, G., Halasa, T., Toft, N., Nielsen, S.S., 2013. Temporal characterisation of the network of Danish cattle movements and its implication for disease control: 2000–2009. Preventive Veterinary Medicine 110, 379-387.

Natale, F., Giovannini, A., Savini, L., Palma, D., Possenti, L., Fiore, G., Calistri, P., 2009. Network analysis of Italian cattle trade patterns and evaluation of risks for potential disease spread. Preventive Veterinary Medicine 92, 341-350.

Natale, F., Savini, L., Giovannini, A., Calistri, P., Candeloro, L., Fiore, G., 2011. Evaluation of risk and vulnerability using a Disease Flow Centrality measure in dynamic cattle trade networks. Preventive Veterinary Medicine 98, 111 - 118.

Negrón, M., Raizman, E.A., Pogranichniy, R., Hilton, W.M., Lévy, M., 2011. Survey on management practices related to the prevention and control of bovine viral diarrhea virus on dairy farms in Indiana, United States. Preventive Veterinary Medicine 99, 130-135.

Neill, S., Hanna, J., O'Brien, J., McCracken, R., 1989. Transmission of tuberculosis from experimentally infected cattle to in-contact calves. Veterinary Record 124, 269 - 271.

Nespeca, R., Vaillancourt, J.-P., Morrow, W.E.M., 1997. Validation of a poultry biosecurity survey. Preventive Veterinary Medicine 31, 73-86.

Newman, M.E.J., 2001. Clustering and preferential attachment in growing networks. Physical Review E 64, e025102.

Newman, M.E.J., 2002. Assortative Mixing in Networks. Physical Review Letters 89, e208701.

Newman, M.E.J., 2003. Properties of highly clustered networks. Physical Review E 68, e026121.

Newman, M.E.J., 2004a. Analysis of weighted networks. Physical Review E 70, e056131.

Newman, M.E.J., 2004b. Fast algorithm for detecting community structure in networks. Physical Review E 69, e066133.

Newman, M.E.J., 2006. Finding community structure in networks using the eigenvectors of matrices. Physical Review E 74, e036104.

Newman, M.E.J., Girvan, M., 2004. Finding and evaluating community structure in networks. Physical Review E 69, e026113.

Nielen, M., Jalvingh, A.W., Horst, H.S., Dijkhuizen, A.A., Maurice, H., Schut, B.H., van Wuijckhuise, L.A., de Jong, M.F., 1996. Quantification of contacts between Dutch farms to assess the potential risk of foot-and-mouth disease spread. Preventive Veterinary Medicine 28, 143-158.

Nielsen, S.S., Toft, N., 2008. Ante mortem diagnosis of paratuberculosis: A review of accuracies of ELISA, interferon-γ assay and faecal culture techniques. Veterinary Microbiology 129, 217-235.

Nishiura, H., Cook, R., Cowling, B., 2011. Assortativity and the probability of epidemic extinction: a case study of pandemic influenza A (H1N1-2009). Interdisciplinary Perspectives on Infectious Diseases 2011, e194507.

Niskanen, R., 1993. Relationship between the levels of antibodies to bovine viral diarrhoea virus in bulk tank milk and the prevalence of cows exposed to the virus. Veterinary Record 133, 341 - 344.

Niskanen, R., Emanuelson, U., Sundberg, J., Larsson, B., Alenius, S., 1995. Effects of infection with bovine virus diarrhoea virus on health and reproductive performance in 213 dairy herds in one county in Sweden. Preventive Veterinary Medicine 23, 229-237.

Niskanen, R., Lindberg, A., 2003. Transmission of Bovine Viral Diarrhoea Virus by Unhygienic Vaccination Procedures, Ambient Air, and from Contaminated Pens. The Veterinary Journal 165, 125-130.

Niskansen, R., Lindberg, A., Larsson, B., Alenius, S., 2000. Lack of virus transmission from primarily bovine viral diarrhoea virus (BVDV) infected calves to susceptible peers. Acta Veterinaria Scandinavia 41, 93 - 99.

Norby, B., Bartlett, P.C., Fitzgerald, S.D., Granger, L.M., Bruning-Fann, C.S., Whipple, D.L., Payeur, J.B., 2004. The Sensitivity of Gross Necropsy, Caudal Fold and Comparative Cervical Tests for the Diagnosis of Bovine Tuberculosis. Journal of Veterinary Diagnostic Investigation 16, 126-131.

Nöremark, M., Hakansson, N., Lindström, T., Wennergren, U., Lewerin, S., 2009. Spatial and temporal investigations of reported movements, births and deaths of cattle and pigs in Sweden. Acta Veterinaria Scandinavica 51, 37.

Nöremark, M., Hakansson, N., Sternberg Lewerin, S., Lindberg, A., Jonsson, A., 2011. Network analysis of cattle and pig movements in Sweden: measures relevant for disease control and risk based surveillance. Preventive Veterinary Medicine 99, 78 - 90.

Obritzhauser, W., Klemens, F., Josef, K., 2005. BVDV infection risk in the course of the voluntary BVDV eradication program in Styria/Austria. Preventive Veterinary Medicine 72, 127 - 132.

Ohlson, A., Heuer, C., Lockhart, C., Traven, M., Emanuelson, U., Alenius, S., 2010. Risk factors for seropositivity to bovine coronavirus and bovine respiratory syncytial virus in dairy herds. Veterinary Record 167, 201-207.

Olea-Popelka, F.J., Costello, E., White, P., McGrath, G., Collins, J.D., O'Keefe, J.O., Kelton, D.F., Berke, O., More, S., Martin, S.W., 2008. Risk factors for disclosure of additional tuberculosis cattle in attested-clear herds that had one animal with a confirmed lesion of tuberculosis at slaughter during 2003 in Ireland. Preventive Veterinary Medicine 85, 81 - 91.

Oliver, S.P., Murinda, S.E., Jayarao, B.M., 2011. Impact of Antibiotic Use in Adult Dairy Cows on Antimicrobial Resistance of Veterinary and Human Pathogens: A Comprehensive Review. Foodborne pathogens and disease 8, 337 - 355.

Ortiz-Pelaez, A., Pfeiffer, D., 2008. Use of data mining techniques to investigate disease risk classification as a proxy for compromised biosecurity of cattle herds in Wales. BMC Veterinary Research 4, 24.

Ortiz-Pelaez, A., Pfeiffer, D., Tempia, S., Otieno, F.T., Aden, H., Costagli, R., 2010. Risk mapping of Rinderpest sero-prevalence in Central and Southern Somalia based on spatial and network risk factors. BMC Veterinary Research 6, 22.

Ortiz-Pelaez, A., Pfeiffer, D.U., Soares-Magalhães, R.J., Guitian, F.J., 2006. Use of social network analysis to characterize the pattern of animal movements in the initial phases of the 2001 foot and mouth disease (FMD) epidemic in the UK. Preventive Veterinary Medicine 76, 40-55.

Owens, F.N., Gill, D.R., Secrist, D.S., Coleman, S., 1995. Review of some aspects of growth and development of feedlot cattle. Journal of Animal Science 73, 3152-3172.

Paaijmans, M., 2002. Analyse van de rundertuberculose-uitbraak van 1999 in Netherlands. Wageningen UR, The Netherlands.

Paiba, G.A., Roberts, S.R., Houston, C.W., Williams, E.C., Smith, L.H., Gibbens, J.C., Holdship, S., Lysons, R., 2007. UK surveillance: Provision of quality assured information from combined datasets. Preventive Veterinary Medicine 81, 117-134.

Palfi, V., Houe, H., Philipsen, J., 1993. Studies on the decline of bovine virus diarrhoea virus (BVDV) maternal antibodies and detectability of BVDV in persistently infected calves. Acta Veterinaria Scandinavica 34, 105 - 107.

Pastor-Satorras, R., Vespignani, A., 2002. Epidemic dynamics in finite size scale-free networks. Physical Review E 65, e035108.

Pautasso, M., Moslonka-Lefebvre, M., Jeger, M.J., 2010. The number of links to and from the starting node as a predictor of epidemic size in small-size directed networks. Ecological Complexity 7, 424-432.

Pavlik, I., 2006. The experience of new European Union Member States concerning the control of bovine tuberculosis. Veterinary Microbiology 112, 221-230.

Perez, A.M., Ward, M.P., Torres, P., Ritacco, V., 2002. Use of spatial statistics and monitoring data to identify clustering of bovine tuberculosis in Argentina. Preventive Veterinary Medicine 56, 63-74.

Perrin, J.-B., Ducrot, C., Vinard, J.-L., Morignat, E., Calavas, D., Hendrikx, P., 2012. Assessment of the utility of routinely collected cattle census and disposal data for syndromic surveillance. Preventive Veterinary Medicine 105, 244-252.

Pillars, R.B., Groom, D.L., 2002. Serologic evaluation of five unvaccinated heifers to detect herds that have cattle persistently infected with bovine viral diarrhea virus. American Journal of Veterinary Research 63, 499 - 505.

Plucinski, M.M., Starfield, R., Almeida, P.P., 2011. Inferring social network structure from bacterial sequence data. PLoS ONE 6, e22685.

Pollock, J.M., Welsh, M.D., McNair, J., 2005. Immune responses in bovine tuberculosis: Towards new strategies for the diagnosis and control of disease. Veterinary Immunology and Immunopathology 108, 37-43.

Pons, P., Latapy, M., 2005. Computing communities in large networks using random walks. Available at: http://arxiv.org/abs/physics/0512106.

R-Development-Core-Team, 2010. R: A language and environment for statistical computing. R Foundation for Statistical Computing.

Raboisson, D., Delor, F., Cahuzac, E., Gendre, C., Sans, P., Allaire, G., 2013. Perinatal, neonatal, and rearing period mortality of dairy calves and replacement heifers in France. Journal of Dairy Science.

Radunz, B., 2006. Surveillance and risk management during the latter stages of eradication: Experiences from Australia. Veterinary Microbiology 112, 283-290.

Ramírez-Villaescusa, A.M., Medley, G.F., Mason, S., Green, L.E., 2008. Herd and individual animal risks associated with bovine tuberculosis skin test positivity in cattle herds in south west England. Preventive Veterinary Medicine 92, 188 - 198.

Ramírez-Villaescusa, A.M., Medley, G.F., Mason, S., Green, L.E., 2010. Risk factors for herd breakdown with bovine tuberculosis in 148 cattle herds in the south west of England. Preventive Veterinary Medicine 95, 224-230.

Rautureau, S., Dufour, B., Durand, B., 2010. Vulnerability of animal trade networks to the spread of infectious diseases: a methodological approach applied to evaluation and emergency control strategies in cattle, France, 2005. Transboundary and Emerging Diseases 58, 110 - 120.

Rautureau, S., Dufour, B., Durand, B., 2012. Structural vulnerability of the French swine industry trade network to the spread of infectious disease. Animal 6, 1152 - 1162.

Reilly, L.A., Courtenay, O., 2007. Husbandry practices, badger sett density and habitat composition as risk factors for transient and persistent bovine tuberculosis on UK cattle farms. Preventive Veterinary Medicine 80, 129 - 142.

Ridge, S.E., Baker, I.M., Hannah, M., 2005. Effect of compliances with recommended calf-rearing practices on control of bovine Johne's disease. Australian Veterinary Journal 83, 85 - 90.

Risau-Gusman, S., Zanette, D.H., 2009. Contact switching as a control strategy for epidemic outbreaks. Journal of Theoretical Biology 257, 52-60.

Robinson, S., Christley, R., 2006. Identifying temporal variation in reported births, deaths and movements of cattle in Britain. BMC Veterinary Research 2, 11.

Robinson, S.E., Christley, R.M., 2007. Exploring the role of auction markets in cattle movements within Great Britain. Preventive Veterinary Medicine 81, 21-37.

Robinson, S.E., Everett, M.G., Christley, R.M., 2007. Recent network evolution increases the potential for large epidemics in the British cattle population. Journal of the Royal Society Interface 4, 669 - 674.

Rossmanith, W., Janacek, R., Wilhelm, E., 2005. Control of BVDV-infection on common grassland—The key for successful BVDV-eradication in Lower Austria. Preventive Veterinary Medicine 72, 133-137.

Roughsedge, T., Amer, P.R., Simm, G., 2003. A bioeconomic model for the evaluation of breeds and mating systems in beef production enterprises. Animal Science 77, 403 - 416.

Rüfenacht, J., Schaller, P., Strasser, M., Perterhans, E., Audige, L., 2000. Prevalence of cattle infected with bovine viral diarrhea virus in Switzerland. Veterinary Record 147, 413 - 417.

Rüfenacht, J., Schaller, P., Audigé, L., Knutti, B., Küpfer, U., Peterhans, E., 2001. The effect of infection with bovine viral diarrhea virus on the fertility of Swiss dairy cattle. Theriogenology 56, 199-210.

Salathé, M., Jones, J.H., 2010. Dynamics and control of diseases in networks with community structure. PLOS Computational Biology 6, e1000736.

Sanson, R.L., Struthers, G., King, P., Weston, J.F., Morris, R.S., 1993. The potential extent of transmission of foot-and-mouth disease: A study of the movement of animals and materials in Southland, New Zealand. New Zealand Veterinary Journal 41, 21-28.

Santarossa, J.M., Stott, A.W., Humphry, R.W., Gunn, G.J., 2005. Optimal risk management versus willingness to pay for BVDV control options. Preventive Veterinary Medicine 72, 183-187.

Santarossa, J.M., Stott, A.W., Woolliams, J.A., Brotherstone, S., Wall, E., Coffey, M.P., 2004. An economic evaluation of long-term sustainability in the dairy sector. Animal Science 79, 315 - 325.

Sarrazin, S., Veldhuis, A., Méroc, E., Vangeel, I., Laureyns, J., Dewulf, J., Caij, A.B., Piepers, S., Hooyberghs, J., Ribbens, S., Van Der Stede, Y., 2013. Serological and virological BVDV prevalence and risk factor analysis for herds to be BVDV seropositive in Belgian cattle herds. Preventive Veterinary Medicine 108, 28 - 37.

Savill, N.J., Shaw, D.J., Deardon, R., Tildesley, M.J., Keeling, M.J., Woolhouse, M.E.J., Brooks, S.P., Grenfell, B.T., 2007. Effect of data quality on estimates of farm infectiousness trends in the UK 2001 foot-and-mouth disease epidemic. Journal of the Royal Society Interface 4, 235-241.

Schepers, J.A., Dijkhuizen, A.A., 1991. The economics of mastitis and mastitis control in dairy cattle: a critical analysis of estimates published since 1970. Preventive Veterinary Medicine 10, 213-224.

Schiller, I., RayWaters, W., Vordermeier, H.M., Jemmi, T., Welsh, M., Keck, N., Whelan, A., Gormley, E., Boschiroli, M.L., Moyen, J.L., Vela, C., Cagiola, M., Buddle, B.M., Palmer, M., Thacker, T., Oesch, B., 2011. Bovine tuberculosis in Europe from the perspective of an officially tuberculosis free country: Trade, surveillance and diagnostics. Veterinary Microbiology 151, 153-159.

Schley, D., Gubbins, S., Paton, D.J., 2009. Quantifying the Risk of Localised Animal Movement Bans for Foot-and-Mouth Disease. PLoS ONE 4, e5481.

Scott, A., Zepeda, C., Garber, L., Smith, J., Swayne, D., Rhorer, A., Kellar, J., Shimshony, A., Batho, H., Caporale, V., Giovannini, A., 2006. The concept of compartmentalisation. Revue scientifique et technique (International Office of Epizootics) 25, 873 - 879.

Serrano, M.A., Boguna, M., 2005. Weighted configuration model. AIP Conference Proceedings 776, 101.

Shirley, M.D.F., Rushton, S.P., 2005. The impacts of network topology on disease spread. Ecological Complexity 2, 287-299.

Shirley, M.W., Charleston, B., King, D.P., 2011. New opportunities to control livestock diseases in the post-genomics era. Journal of Agricultural Science 149, 115 - 121.

Simini, F., Gonzalez, M.C., Maritan, A., Barabasi, A.-L., 2012. A universal model for mobility and migration patterns. Nature 484, 96 - 100.

Slingenbergh, J., Gilbert, M., de Balogh, K., Wint, W., 2004. Ecological sources of zoonotic disease. Revue scientifique et technique (International Office of Epizootics) 23, 467 - 484.

Smith, A.K., Ayanian, J.Z., Covinsky, K.E., Landon, B.E., McCarthy, E.P., Wee, C.C., Steinman, M.A., 2011. Conducting high-value secondary dataset analysis: an introductory guide and resources. Journal of General Internal Medicine 26, 920 - 929.

Smith, D.R., Grotelueschen, D.M., 2004. Biosecurity and biocontainment of bovine viral diarrhea virus. Veterinary Clinics of North America: Food Animal Practice 20, 131-149.

Sol, J., Stelwagen, J., Dijkhuizen, A., 1984. A three year herd health and management program on thirty Dutch dairy farms. II. Culling strategies and losses caused by forced replacement of dairy cows. Veterinary Quarterly 6, 149 - 157.

Sorge, U., Kelton, D., Lissemore, K., Godkin, A., Hendrick, S., Wells, S., 2010. Attitudes of Canadian dairy farmers toward a voluntary Johne's disease control program. Journal of Dairy Science 93, 1491-1499.

Soumaré, B., Thys, E., Berkvens, D., Hashi, A., Van Huylenbroeck, G., 2006. Effects of livestock import bans imposed by Saudi Arabia on Somaliland for sanitary reasons related to Rift Valley fever. Outlook on Agriculture 35, 19-24.

Sprecher, D.J., Baker, J.C., Holland, R.E., Yamini, B., 1991. An outbreak of fetal and neonatal losses associated with the diagnosis of bovine viral diarrhea virus. Theriogenology 36, 597-606.

Stack, J.C., Bansal, S., Kumar, V.S.A., Grenfell, B., 2013. Inferring population-level contact heterogeneity from common epidemic data. Journal of The Royal Society Interface 10, In Press.

Stark, K., Regula, G., Hernandez, J., Knopf, L., Fuchs, K., Morris, R., Davies, P., 2006. Concepts for risk-based surveillance in the field of veterinary medicine and veterinary public health: Review of current approaches. BMC Health Services Research 6, 20.

Stott, A.W., 2003. Costs and Benefits of Preventing Animal Diseases: A review focusing on endemic diseases. Scottish Agricultural College. Available at: http://www.scotland.gov.uk/Publications/2005/01/20496/49533

Stott, A.W., Gunn, G.J., 2008. Use of a benefit function to assess the relative investment potential of alternative farm animal disease prevention strategies. Preventive Veterinary Medicine 84, 179-193.

Stott, A.W., Jones, G.M., Humphry, R.W., Gunn, G.J., 2005. Financial incentive to control paratuberculosis (Johne's disease) on dairy farms in the United Kingdom. Veterinary Record 156, 825 - 831.

Stott, A.W., Lloyd, J., Humphry, R.W., Gunn, G.J., 2003. A linear programming approach to estimate the economic impact of bovine viral diarrhoea (BVD) at the whole-farm level in Scotland. Preventive Veterinary Medicine 59, 51-66.

Stott, A.W., Veerkamp, R.F., Wassell, T.R., 1999. The economics of fertility in the dairy herd. Animal Science 68, 49 - 57.

Ståhl, K., Kampa, J., Baule, C., Isaksson, M., Moreno-López, J., Belák, S., Alenius, S., Lindberg, A., 2005. Molecular epidemiology of bovine viral diarrhoea during the final phase of the Swedish BVD-eradication programme. Preventive Veterinary Medicine 72, 103-108.

Ståhl, K., Lindberg, A., Rivera, H., Ortiz, C., Moreno-López, J., 2008. Self-clearance from BVDV infections—A frequent finding in dairy herds in an endemically infected region in Peru. Preventive Veterinary Medicine 83, 285-296.

Svensson, C., Lundborg, K., Emanuelson, U., Olsson, S.-O., 2003. Morbidity in Swedish dairy calves from birth to 90 days of age and individual calf-level risk factors for infectious diseases. Preventive Veterinary Medicine 58, 179-197.

Talafha, A.Q., Hirche, S.M., Ababneh, M.M., Al-Majali, M.M., Ababneh, M.M., 2009. Prevalence and risk factors associated with bovine viral diarrhea virus infection in dairy herds in Jordan. Tropical Animal Health and Production 41, 499 - 506.

Taylor, L., Janzen, E., Ellis, J., Van den Hurk, J., Ward, P., 1997. Performance, survival, necropsy, and virological findings from calves persistently infected with the bovine viral diarrhea virus originating from a single Saskatchewan beef herd. Canadian Vetetrinary Journal 38, 29 - 37.

Tero, A., Takagi, S., Saigusa, T., Ito, K., Bebber, D.P., Fricker, M.D., Yumiki, K., Kobayashi, R., Nakagaki, T., 2010. Rules for Biologically Inspired Adaptive Network Design. Science 327, 439-442.

Thobokwe, G., Heuer, C., Hayes, D.P., 2004. Validation of a bulk tank milk antibody ELISA to detect dairy herds likely infected with bovine viral diarrhoea virus in New Zealand. New Zealand Veterinary Journal 52, 394 - 400.

Thomsen, P.T., Kjeldsen, A.M., Sorensen, J.T., Houe, H., Ersbøll, A.K., 2006. Herd-level risk factors for the mortality of cows in Danish dairy herds. Veterinary Record 158, 622 - 626.

Thornton, P.K., 2010. Livestock production: recent trends, future prospects. The Royal Society B: Biological Sciences 365, 2853-2867.

Tildesley, M.J., Deardon, R., Savill, N.J., Bessell, P.R., Brooks, S.P., Woolhouse, M.E.J., Grenfell, B.T., Keeling, M.J., 2008. Accuracy of models for the 2001 foot-and-mouth epidemic. Proceedings. Biological sciences / The Royal Society 275, 1459-1468.

Tildesley, M.J., Savill, N.J., Shaw, D.J., Deardon, R., Brooks, S.P., Woolhouse, M.E.J., Grenfell, B.T., Keeling, M.J., 2006. Optimal reactive vaccination strategies for a foot-and-mouth outbreak in the UK. Nature 440, 83 - 86.

Tildesley, M.J., Volkova, V.V., Woolhouse, M.E.J., 2011. Potential for epidemic take-off from the primary outbreak farm via livestock movements. BMC Veterinary Research 7, 76.

Tinsley, M., Lewis, F.I., Brulisauer, F., 2012. Network modeling of BVD transmission. Veterinary Research 43, 11.

Tiwari, A., VanLeeuwen, J.A., Dohoo, I.R., Stryhn, H., Keefe, G.P., Haddad, J.P., 2005. Effects of seropositivity for bovine leukemia virus, bovine viral diarrhoea virus, Mycobacterium avium subspecies paratuberculosis, and Neospora caninum on culling in dairy cattle in four Canadian provinces. Veterinary Microbiology 109, 147-158.

Toma, L., Stott, A.W., Heffernan, C., Ringrose, S., Gunn, G.J., 2013. Determinants of biosecurity behaviour of British cattle and sheep farmers—A behavioural economics analysis. Preventive Veterinary Medicine 108, 321 - 333.

Tozer, P.R., Heinrichs, A.J., 2001. What affects the costs of raising replacement dairy heifers: a multiple-component analysis. Journal of Dairy Science 84, 1836 - 1844.

Truyers, I.G.R., Mellor, D.J., Norquay, R., Gunn, G.J., Ellis, K.A., 2010. Eradication programme for bovine viral diarrhoea virus in Orkney 2001 to 2008. Veterinary Record 167, 566 - 570.

Tråvén, M., Alenius, S., Fossum, C., Larsson, B., 1991. Primary Bovine Viral Diarrhoea Virus Infection in Calves Following Direct Contact with a Persistently Viraemic Calf. Journal of Veterinary Medicine, Series B 38, 453-462.

Turner, J., Bowers, R.G., Clancy, D., Behnke, M.C., Christley, R.M., 2008. A network model of E. coli O157 transmission within a typical UK dairy herd: The effect of heterogeneity and clustering on the prevalence of infection. Journal of Theoretical Biology 254, 45-54.

Uetake, K., 2013. Newborn calf welfare: A review focusing on mortality rates. Animal Science Journal 84, 101-105.

Valle, P.S., Martin, S.W., Tremblay, R., Bateman, K., 1999. Factors associated with being a bovine-virus diarrhoea (BVD) seropositive dairy herd in the Møre and Romsdal County of Norway. Preventive Veterinary Medicine 40, 165-177.

Valle, P.S., Skjerve, E., Martin, S.W., Larssen, R.B., Østerås, O., Nyberg, O., 2005. Ten years of bovine virus diarrhoea virus (BVDV) control in Norway: a cost-benefit analysis. Preventive Veterinary Medicine 72, 189-207.

Valle, P.S., Wayne Martin, S., Skjerve, E., 2001. Time to first calving and calving interval in bovine virus diarrhoea virus (BVDV) sero-converted dairy herds in Norway. Preventive Veterinary Medicine 51, 17-36.

Van Arendonk, J.A.M., 1985. Studies on the replacement policies in dairy cattle. II. Optimum policy and influence of changes in production and prices. Livestock Production Science 13, 101-121.

van Asseldonk, M.A.P.M., van Roermund, H.J.W., Fischer, E.A.J., de Jong, M.C.M., Huirne, R.B.M., 2005. Stochastic efficiency analysis of bovine tuberculosis surveillance programs in the Netherlands. Preventive Veterinary Medicine 69, 39 - 52.

Van Kerkhove, M.D., Vong, S., Guitian, J., Holl, D., Mangtani, P., San, S., Ghani, A.C., 2009. Poultry movement networks in Cambodia: Implications for surveillance and control of highly pathogenic avian influenza (HPAI/H5N1). Vaccine 27, 6345-6352.

van Schaik, G., Dijkhuizen, A.A., Huirne, R.B.M., Schukken, Y.H., Nielen, M., Hage, H.J., 1998. Risk factors for existence of Bovine Herpes Virus 1 antibodies on nonvaccinating Dutch dairy farms. Preventive Veterinary Medicine 34, 125-136.

van Schaik, G., Nielen, M., Dijkhuizen, A.A., 2001. An economic model for on-farm decision support of management to prevent infectious disease introduction into dairy farms. Preventive Veterinary Medicine 51, 289-305.

van Schaik, G., Schukken, Y.H., Nielen, M., Dijkhuizen, A.A., Barkema, H.W., Benedictus, G., 2002. Probability of and risk factors for introduction of infectious diseases into Dutch SPF dairy farms: a cohort study. Preventive Veterinary Medicine 54, 279-289.

Van Winden, S., Pfeiffer, D., 2008. Sampling programmes to establish and monitor the infectious disease status of cattle herds. In Practice 30, 30-35.

Van Winden, S., Stevens, K., Guitian, J., Mcgowan, M., 2011. Preliminary findings of a systematic review and expert opinion workshop on biosecurity on cattle farms in the UK. Cattle practice: Journal of the British Cattle Veterinary Association 13, 135-140.

Van Wuijckhuise, L., Bosch, J., Franken, P., Frankena, K., Elbers, A.R.W., 1998. Epidemiological characteristics of bovine herpesvirus 1 infections determined by bulk milk testing of all Dutch dairy herds. Veterinary Record 142, 181-184.

Vargas, B., Herrero, M., van Arendonk, J.A.M., 2001. Interactions between optimal replacement policies and feeding strategies in dairy herds. Livestock Production Science 69, 17-31.

Varo Barbudo, A., Gunn, G.J., Stott, A.W., 2008. Combining models to examine the financial impact of infertility caused by bovine viral diarrhoea in Scottish beef suckler herds. The Journal of Agricultural Science 146, 621 - 632.

Vazquez, A., 2003. Growing network with local rules: Preferential attachment, clustering hierarchy, and degree correlations. Physical Review E 67, e056104.

Velthuis, A.G.J., Mourits, M.C.M., 2007. Effectiveness of movement-prevention regulations to reduce the spread of foot-and-mouth disease in The Netherlands. Preventive Veterinary Medicine 82, 262-281.

Vernon, M.C., 2011. Demographics of cattle movements in the United Kingdom. BMC Veterinary Research 7, 31.

Vernon, M.C., Keeling, M.J., 2009. Representing the UK's cattle herd as static and dynamic networks. Proceedings. Biological sciences / The Royal Society 276, 469-476.

Vernon, M.C., Keeling, M.J., 2012. Impact of regulatory perturbations to disease spread through cattle movements in Great Britain. Preventive Veterinary Medicine 105, 110-117.

Vernon, M.C., Webb, C.R., Heath, M.F., 2010. Postal survey of contacts between cattle farms on the Isle of Lewis. The Veterinary Record 166, 37-40.

Veysset, P., Bebin, D., Lherm, M., 2005. Adaptation to Agenda 2000 (CAP reform) and optimisation of the farming system of French suckler cattle farms in the Charolais area: a model-based study. Agricultural Systems 82, 179 - 202.

Viet, A.-F., Fourichon, C., Seegers, H., Jacob, C., Guihenneuc-Jouyaux, C., 2004. A model of the spread of the bovine viral-diarrhoea virus within a dairy herd. Preventive Veterinary Medicine 63, 211-236.

Volkova, V.V., Howey, R., Savill, N.J., Woolhouse, M.E.J., 2010. Potential for transmission of infections in networks of cattle farms. Epidemics 2, 116-122.

Volz, E.M., Miller, J.C., Galvani, A., Ancel Meyers, L., 2011. Effects of heterogeneous and clustered contact patterns on infectious disease dynamics. PLoS Computational Biology 7, e1002042.

Von Bailey, D., Hunnicutt, L., 2002. The role of transaction costs in market selection: market selection in commercial feeder cattle operations. Annual Meeting of the American Agricultural Economics Association. Long Beach, CA, USA.

Vonk Noordegraaf, A., Buijtels, J.A.A.M., Dijkhuizen, A.A., Franken, P., Stegeman, J.A., Verhoeff, J., 1998. An epidemiological and economic simulation model to evaluate the spread and control of infectious bovine rhinotracheitis in the Netherlands. Preventive Veterinary Medicine 36, 219-238.

Waret-Szukuta, A., Ortiz-Pelaez, A., Pfeiffer, D.U., Roger, F., Guitian, F.J., 2010. Herd contact structure based on shared water points and grazing points in the Highlands of Ethiopia. Epidemiology and Infection 139, 875-885.

Wathes, D.C., Brickell, J.S., Bourne, N.E., Swali, A., Cheng, Z., 2008. Factors influencing heifer survival and fertility on commercial dairy farms. Animal 2, 1135 - 1143.

Watts, D.J., Strogatz, S.H., 1998. Collective dynamics of `small-world' networks. Nature 393, 440-442.

Webb, C.R., 2005. Farm animal networks: unraveling the contact structure of the British sheep population. Preventive Veterinary Medicine 68, 3-17.

Weber, M.F., van Roermund, H.J.W., Vernooij, J.C.M., Kalis, C.H.J., Stegeman, J.A., 2006. Cattle transfers between herds under paratuberculosis surveillance in The Netherlands are not random. Preventive Veterinary Medicine 76, 222-236.

Webster, A.J.F., 2001. Farm Animal Welfare: the Five Freedoms and the Free Market. The Veterinary Journal 161, 229-237.

Welby, S., Govaerts, M., Vanholme, L., Hooyberghs, J., Mennens, K., Maes, L., Van Der Stede, Y., 2012. Bovine tuberculosis surveillance alternatives in Belgium. Preventive Veterinary Medicine 106, 152-161.

Weldegebriel, H.T., Gunn, G.J., Stott, A.W., 2009. Evaluation of producer and consumer benefits resulting from eradication of bovine viral diarrhoea (BVD) in Scotland, United Kingdom. Preventive Veterinary Medicine 88, 49-56.

Wells, S.J., 2001. Biosecurity on dairy operations: hazards and risks. Journal of Dairy Science 83, 2380 - 2387.

Wells, S.J., Dargatz, D.A., Ott, S.L., 1996. Factors associated with mortality to 21 days of life in dairy heifers in the United States. Preventive Veterinary Medicine 29, 9-19.

Wentink, G.H., van Exsel, A.C.A., de Goey, I., van Lieshout, J.A.H., 1991. Spread of bovine virus diarrhoea virus in a herd of heifer calves. Veterinary Quarterly 13, 233 - 236.

West, J.W., 2003. Effects of Heat-Stress on Production in Dairy Cattle. Journal of Dairy Science 86, 2131-2144.

Whipple, D.L., Bolin, C.A., Miller, J.M., 1996. Distribution of lesions in cattle infected with Mycobacterium bovis. Journal of Veterinary Diagnostic Investigation 8, 351 - 354.

White, P.C., Benhin, J.K.A., 2004. Factors influencing the incidence and scale of bovine tuberculosis in cattle in southwest England. Preventive Veterinary Medicine 63, 1 - 7.

White, P.C.L., Whiting, S.J., 2000. Public attitudes towards badger culling to control bovine tuberculosis in cattle. Veterinary Record 147, 179 - 184.

Wittum, T.E., Grotelueschen, D.M., Brock, K.V., Kvasnicka, W.G., Floyd, J.G., Kelling, C.L., Odde, K.G., 2001. Persistent bovine viral diarrhoea virus infection in US beef herds. Preventive Veterinary Medicine 49, 83-94.

Wolfe, D.M., Berke, O., Kelton, D.F., White, P.W., More, S.J., O'Keeffe, J., Martin, S.W., 2010. From explanation to prediction: a model for recurrent bovine tuberculosis in Irish cattle herds. Preventive Veterinary Medicine 94, 170 - 177.

Wolfe, D.M., Berke, O., More, S.J., Kelton, D.F., White, P.W., O'Keeffe, J.J., Martin, S.W., 2009. The risk of a positive test for bovine tuberculosis in cattle purchased from herds with and without a recent history of bovine tuberculosis in Ireland. Preventive Veterinary Medicine 92, 99-105.

Wolfova, M., Wolf, J., Pribyl, J., Zahradkova, R., Kica, J., 2005. Breeding objectives for beef cattle used in different production systems: 1. Model development. Livestock Production Science 95, 201 - 215.

Woodbine, K.A., Medley, G.F., Moore, S.J., Ramirez-Villaescusa, A.M., Mason, S., Green, L.E., 2009a. A four year longitudinal sero-epidemiological study of bovine herpesvirus type-1 (BHV-1) in adult cattle in 107 unvaccinated herds in south west England. BMC Veterinary Research 5, 5.

Woodbine, K.A., Schukken, Y.H., Green, L.E., Ramirez-Villaescusa, A., Mason, S., Moore, S.J., Bilbao, C., Swann, N., Medley, G.F., 2009b. Seroprevalence and epidemiological characteristics of Mycobacterium avium subsp. paratuberculosis on 114 cattle farms in south west England. Preventive Veterinary Medicine 89, 102-109.

Woolhouse, M., 2011. How to make predictions about future infectious disease risks. Philosophical Transactions of the Royal Society B: Biological Sciences 366, 2045 - 2054.

Woolhouse, M.E., Dye, C., Etard, J.F., Smith, T., Charlwood, J.D., Garnett, G.P., Hagan, P., Hii, J.L., Ndhlovu, P.D., Quinnell, R.J., Watts, C.H., Chandiwana, S.K., Anderson, R.M., 1997. Heterogeneities in the transmission of infectious agents: implications for the design of control programs. Proceedings of the National Academy of Sciences 94, 338-342.

Woolhouse, M.E., Shaw, D.J., Matthews, L., Liu, W.C., Mellor, D.J., Thomas, M.R., 2005. Epidemiological implications of the contact network structure for cattle farms and the 20-80 rule. Biology Letters 1, 350-352.

Wraight, M.D., McNeil, J., Beggs, D.S., Greenall, R.K., Humphris, T.B., Irwin, R.J., Jagoe, S.P., Jemmeson, A., Morgan, W.F., Brightling, P., Anderson, G.A., Mansell, P.D., 2000. Compliance of Victorian dairy farmers with current calf rearing recommendations for control of Johne's disease. Veterinary Microbiology 77, 429-442.

Yancey Jr, R.J., 1999. Vaccines and diagnostic methods for bovine mastitis: fact and fiction. Advances in Veterinary Medicine 41, 257-273.

Youngquist, R.S., Threllfall, W., 1997. Current therapy in large animal theriogenology. WB Saunders Company Philadelphia.

Zadoks, R.N., Allore, H.G., Barkema, H.W., Sampimon, O.C., Wellenberg, G.J., Gröhn, Y.T., Schukken, Y.H., 2001. Cow- and quarter-level risk factors for Streptococcus uberis and Staphylococcus aureus mastitis. Journal of Dairy Science 84, 2649-2663.

Appendix A

BVDV Beef Management Survey

BVD Prevalence Study – Questionnaire

COVER SHEET

Applicable sections of the cover sheet might be completed in advance of the interview

Interview details	
Name of interviewer	
Date of interview	

Farmer's details	
Farm ID code (Ref no from list of farms)	
First name	
Last name	
Address	
Town/village	
Postcode	
Telephone number	

How many holding numbers does the farmer have for his cattle (including dairy) enterprises?	

Does the farmer want feedback on test results?	Yes	No
IF 'Yes' please provide name and address of farmers vet		
Name		
Address		
Town/village		
Postcode		
Telephone number		

Is the farmer prepared to help in future work?	Yes	No	Don't know

TO BE FILLED IN BY LAB PERSONNEL:

Submission Number	

FARM DETAILS

Questions refer to the **beef** enterprise on the farm only
Could you please provide the average number of each beef cattle-type held on the farm

	Cattle type	*Number*
1	Suckler cows	
2	Calves	
3	Breeding bulls	
4	Cattle for finishing	
5	Stores	
6	Replacement heifers	

Please provide the average yearly number of cattle **introduced into the herd** for each beef cattle-type

	Cattle type	*Number*	*Type of source (eg. mart, dealer, other farmer)*
7	Suckler cows (for replacement)		
8	Stores (for fattening)		
9	In calf heifers (for replacement)		
10a	Newborn calves (for suckling)		
10b	Weaned calves (for fattening)		
11	Bulls		
	Other (please specify below)		
12			
13			

Please provide the following farm business characteristics (tick relevant box)

	Farm characteristics	*Yes*	*No*
14	Is all the grazing land contained within a single farm boundary?		
15	Are any beef cattle **grazed** outwith the main farm boundaries?		
16	Are any beef cattle **housed** outwith the main farm boundaries?		
17	Are beef cattle the main farm enterprise?		
18	Are cattle sold as finishers?		
19	Are cattle sold as stores?		
20	Are cattle sold as breeding stock?		
21	Is the herd pedigree?		
22	Do your beef cattle attend shows?		
23	Do you operate a dairy enterprise?		
24	Does the farm have a sheep enterprise?		
25	Do you ever see deer grazing in close proximity to your cattle?		

		Yes	*No*	*Don't know*
26	Do you think your beef cattle may be affected by BVD?			
27	Have you had a BVD persistently infected (PI) animal in the last five years?			

MANAGEMENT PRACTICES

Questions refer to the **beef** enterprise on the farm only
Please tick the relevant box and provide further information for questions 29b, 38b & 46b

	Management practice	*Yes*	*No*
28a	Do you ever buy in, borrow, or hire cattle, including bulls?		
28b	IF YES, do you only bring in cattle from BVD accredited herds?		
28c	IF YES do you carry out blood and/or other diagnostic screening at purchase?		
28d	IF YES, do you vaccinate purchased stock for BVD?		
29a	Do you implement an isolation period for introduced livestock?		
29b	IF YES, how long is the isolation period? *days*		
30	Do you restrict access of non-essential visitors around the farm?		
31	Do you enforce strict disinfection measures for essential visitors (e.g. vets, AI)?		
32	Do you provide a dedicated pick-up/drop-off area for delivery and pick-up vehicles which serve only this purpose?		
33	Do public footpaths or rights of way cross your farm?		
34	Are your cattle able to drink from a pond shared with another livestock farm or a watercourse downstream from a nearby livestock farm?		
35	Are all grazing areas sharing a boundary with a neighbouring livestock farm fully double fenced to prevent nose to nose contact?		
36	Do you ever use relief stock-people who come into contact with livestock from other farms?		
37	Are all feedstores, silage clamps and cattle buildings deer-proof?		
38a	Do you routinely vaccinate your herd for BVD?		
38b	IF YES, when did you last vaccinate? *months ago*		
39	Do you ever use artificial insemination (AI)?		
40	Do you ever use a bull?		
41	Do you ever use embryo transfer (ET)?		
42a	Are your cattle ever housed?		
42b	IF YES, are pregnant cows or heifers ever housed with calves?		
43	Do you ever share or let pasture?		
44	Do you ever share equipment such as trailers with neighbours?		
45	Does your farm health plan include BVD?		
46a	Is your herd accredited as being BVD-free?		
46b	IF YES, please provide name of scheme		
47a	Do you participate in the Animal Health and Welfare Programme under the Land Management Contract Menu Scheme?		
47b	IF YES, do you take advantage of the following options for BVD control?		
	Biosecurity	Sampling	

Please feel free to make any further comments

Appendix B

BVDV Dairy Management Survey

COLLECTION:
PLEASE STICK FARM IDENTIFICATION CODE HERE

Supporting the land-based industries for over a century

SAC

Epidemiology Research Unit, Inverness

BVD Prevalence Study in Dairy Cattle

	Your name and address			
1	Name			
2	Address			
3				
4	Postcode			
5	Do you want feedback on test results?	Yes	No	
	IF 'Yes' please provide the name and address of your vet so that we can copy the result to the practice			
6	Name			
7	Address			
8				
9	Postcode			

FARM DETAILS

Please provide the average number of each dairy cattle-type held on the farm

	Cattle type	*Number*
10	Dairy cows (in milk)	
11	Dairy cows (dry)	
12	Calves (under 12 months)	
13	Breeding bulls	
14	Replacement heifers (over 12 months)	

Please provide the average yearly number of cattle **introduced into the herd** for each dairy cattle-type

	Cattle type	*Number introduced*	*Type of source (eg. Mart, dealer, other farmer)*
15	Cows and heifers in milk (not in calf)		
16	In calf cows and heifers (in milk or dry)		
17	Dairy calves		
18	Bulls (dairy or beef running with dairy herd)		
19	Other (please specify below)		
20			

Please provide the following farm business characteristics (tick relevant box)

	Farm characteristics	*Yes*	*No*
21	Is all the grazing land contained within a single farm boundary?		
22	Are any dairy cattle **grazed** away from the main homestead?		
23	Are any dairy cattle **housed** away from the main homestead?		
24	Is dairying the main farm enterprise?		
25	Are dairy cattle sold as breeding stock?		
26	Is the dairy herd pedigree?		
27	Do your dairy cattle attend shows?		
28	Do you operate a beef enterprise?		
29	Does the farm have a sheep enterprise?		
30	Do you ever see deer grazing in close proximity to your cattle?		

		Yes	*No*	*Don't know*
31	Do you think your dairy cattle may be affected by BVD?			
32	Have you had a BVD persistently infected (PI) animal in the last five years?			

MANAGEMENT PRACTICES

Questions refer to the **dairy** enterprise on the farm only

Please tick the relevant box and provide further information for questions 34b, 43b & 51b

	Management practice	*Yes*	*No*
33a	Do you ever buy in, borrow, or hire cattle, including bulls?		
33b	IF YES, do you only bring in cattle from BVD accredited herds?		
33c	IF YES do you carry out blood and/or other diagnostic screening at purchase?		
33d	IF YES, do you vaccinate purchased stock for BVD?		
34a	Do you implement an isolation period for introduced livestock?		
34b	IF YES, how long is the isolation period? *days*		
35	Do you restrict access of non-essential visitors around the farm?		
36	Do you enforce strict disinfection measures for essential visitors (e.g. vets, AI)?		
37	Do you provide a separate pick-off/drop-up area for delivery and pick-up vehicles?		
38	Do public footpaths or rights of way cross your farm?		
39	Are your cattle able to drink from a pond shared with another livestock farm or a watercourse downstream from a nearby livestock farm?		
40	Are all grazing areas sharing a boundary with a neighbouring livestock farm fully double fenced to prevent nose to nose contact?		
41	Do you ever use relief stock-people who come into contact with livestock from other farms?		
42	Are all feedstores, silage clamps and cattle buildings deer-proof?		
43a	Do you routinely vaccinate your herd for BVD?		
43b	IF YES, when did you last vaccinate? *months*		
44	Do you ever use artificial insemination (AI)?		
45	Do you ever use a bull?		
46	Do you ever use embryo transfer (ET)?		
47a	Are your cattle ever housed?		
47b	IF YES, are pregnant cows or heifers ever housed with calves?		
48	Do you ever share or let pasture?		
49	Do you ever share equipment such as livestock trailers with neighbours?		
50	Does your farm health plan include BVD?		
51a	Is your herd accredited as being BVD-free?		
51b	IF YES, please provide name of scheme		
52a	Do you participate in the Animal Health and Welfare Programme under the Land Management Contract Menu Scheme?		
52b	IF YES, do you take advantage of the following options for BVD control?		
	Biosecurity	Sampling	

Thank you for your participation. Please feel free to make any comments.

For SAC staff	
LIMS reference number	